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SUBPHRENIC ABSCESS*

A Report of One Hundred and Eleven Consecutive Operative Cases

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THE most satisfactory method of handling an inflammatory process beneath the diaphragm is still a matter of debate, and any clarification of the disputed issues must come as a result of study of a number of cases sufficiently large to be of significance. During the years from 1900 to 1938, inclusive, there have been 175 cases at the Massachusetts General Hospital in which a diagnosis of a subphrenic infectious process has been made (Table 1). In 22 cases, undrained abscesses, usually of secondary importance to other equally lethal diseases, were discovered at autopsy. A study of the clinical course in these cases, however, gives added weight to the findings of Ochsner and DeBakey[1] in a large series of cases assembled from the literature. These demonstrated that collections of pus beneath the diaphragm will terminate in a fatal outcome in approximately 90 per cent of cases unless they are surgically drained.

TABLE 1. *Cases Diagnosed as Subphrenic Abscess or Subphrenic Inflammation.*

CLASSIFICATION OF CASE	NO. OF CASES
Operation for subphrenic drainage	111
No operation ("subphrenic inflammation")	32
No operation for subdiaphragmatic abscess (confirmed at autopsy)	22
Operation but no pus encountered	6
Spontaneously drained via previous operative sinus	4
Total	175

Spontaneous drainage was encountered in 4 cases of this series, in all of which the apparently healed sinus, formed about the wick of a previous laparotomy, served as a guide for the escape of pus imprisoned beneath the diaphragm.

In 32 cases the clinical course, physical findings and x-ray evidence suggested a mild irritative process beneath the diaphragm. All these patients recovered without surgical interference, and a diagnosis of subdiaphragmatic inflammation was made in this selected group in order to differentiate the cases and those with true subphrenic abscess formation.

Six patients, on whom operation was performed but without encountering pus, were presumably suffering from a similar nonsuppurative type of lesion. Thus, in 38 or 22 per cent of the cases there was an inflammatory process beneath the diaphragm for which no surgical intervention was indicated. Undoubtedly there were an indeterminate number of cases falling into this same category that were never recorded as subdiaphragmatic inflammation because of the surgeon's unwillingness to make a diagnosis which could not be confirmed. Lee[2] points out in reporting a selected number of these same cases that the occurrence of subphrenic inflammation subsiding without operation is not a rare finding. Ochsner and Graves[3] state that over two thirds of all subphrenic infections subside without suppuration, and I suspect that their estimate more nearly approaches the true incidence of this condition than does the 22 per cent given above in connection with the present series.

ANATOMY

Martinet[4] in France and Barnard[5] in England, at the beginning of this century, first accurately described the subphrenic spaces, and since that time it has generally come to be accepted that the term "subphrenic" as used to designate the localization of an abscess refers not alone to the region immediately below the diaphragm, but includes as well an area that extends as far down as the transverse colon. If this more comprehensive space be considered, it will be seen that it is subdivided by the ligaments of the liver and the adjacent structures. To the right of the falciform suspensory ligament, and bounded by the liver edge below, lie the right anterior and right postero-

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superior spaces, separated by the cardinal ligament of the liver and its lateral extension (Figs. 1 and 2). The anterior space is by far the larger of the two because of the decidedly posterior position of this ligament. Between the leaves of the ligament and abutting on the peritoneal cavity, but not actually within it, is a distinct and separate area which is extraperitoneal, and may represent the confines

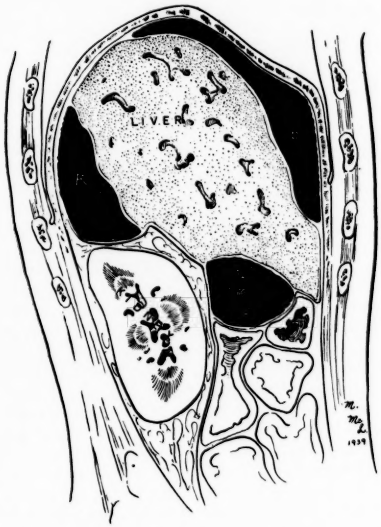

FIGURE 1. *Sagittal View of the Right Abdomen.*

This shows the relative sites of abscesses occurring in the three most commonly involved subphrenic spaces. A—*right posterosuperior;* B—*right anterosuperior;* C—*right inferior.*

of a subphrenic abscess or the extension of a process from one of the adjacent spaces. The right inferior space is bounded by the kidney posteriorly, the undersurface of the liver above, the round ligament and the ligament of the ductus venosus medially, and the transverse colon below. In addition to these divisions on the right, a potential retroperitoneal space exists between the diaphragm and the diaphragmatic peritoneum that may become distended with pus from a dissecting retroperitoneal infection. In this series the latter space played a relatively minor role.

The left subphrenic area is far less commonly involved than is the right, there being only 13 per cent of this series in which an abscess was found to the left of the midline. On this side there are again three spaces, but because of the extreme posterior position of the left lateral ligament there is but a single superior space. The left posteroinferior space is the lesser peritoneal cavity, while the left anterior space is bounded by the liver above, the stomach below and the gastrohepatic omentum posteriorly.

It is a lack of familiarity with these constant anatomic spaces that often leads to an unwise selection of approach for drainage, and to an unfortunate hesitancy in the actual execution of the operation. That a certain amount of ambiguity exists in the minds of some surgeons regarding these spaces is not surprising, because of the relative infrequency with which any one surgeon is called on to differentiate them. In this series, the greatest number of cases drained by any individual was only 10, and fifty-two different operators were responsible for the surgical treatment of the 111 cases reported.

Age Incidence and Sex Distribution

The age incidence in the 111 operative cases of subphrenic abscess showed a steady increase from the first to the fifth decade, the average age for the group as a whole being thirty-eight years (Table 2). The youngest patient was three years

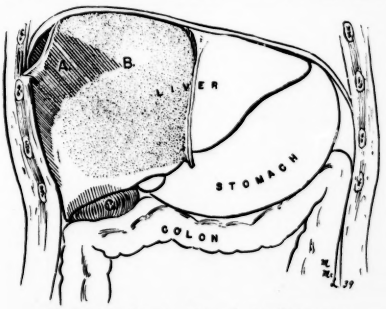

FIGURE 2. *Anterior View of the Abdomen.*

This shows the relative sites of abscesses occurring in the three most commonly involved subphrenic spaces. A—*right posterosuperior;* B—*right anterosuperior;* C—*right inferior. The shaded portions of* A *and* C *are actually not visible in this view as they lie behind the substance of the liver.*

old and the oldest was seventy-six. As regards the distribution of the sexes, 68 of the patients (61 per cent) were men.

Etiology

Although certain subphrenic infections undoubtedly gain access to the subdiaphragmatic area by way of the lymphatics and the blood stream, the

vast majority originate from an extension of intraperitoneal sepsis. Such extension up the lateral gutter is favored by the presence in the upper abdomen of a negative pressure fluctuating with respiration, as demonstrated by Overholt.[6] In addition to this factor, the ventral curvature of the lumbar spine with the patient in the supine position results in a transverse ridge that favors the gravitation of pus distally into the pelvis and proximally into the subdiaphragmatic region.

TABLE 2. *Incidence According to Decades.*

Age	No. of Cases	Per Cent of Total Cases
yr.		
0–10	6	5
10–20	12	11
20–30	15	13
30–40	25	23
40–50	23	21
50–60	23	21
60 and over	7	6
Total	111	

Infection originating in the appendix, as shown in Figure 3, is the commonest source of subphrenic abscess formation, and was responsible for 31 per cent of the cases in this series.

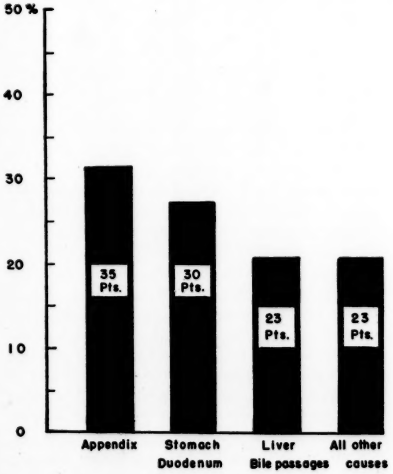

FIGURE 3. *Etiology of Subphrenic Abscess.*

Second in importance as the primary source of infection were lesions in the stomach and duodenum, responsible for 27 per cent of the abscesses, while those in the liver and bile passages, with 21 per cent, ranked third. All other sources combined (21 per cent) individually played very minor roles as etiologic factors. In the collected series of cases reported by Ochsner and DeBakey,[1] and already referred to, the order of importance in the inciting causes was found to be the same.

Diagnosis

The presence of a subphrenic abscess should be suspected in any patient with a persistent unexplained fever associated with a history of recent intraperitoneal sepsis. It should be borne in mind that not infrequently (in 26 per cent of these cases) the inciting cause is never clearly established, although in most cases in this series (64 per cent) an antecedent laparotomy had either confirmed the presence of a septic focus, or had itself proved to be a source of untoward peritoneal contamination. Ten per cent of the patients had had no operation preceding the drainage of their abscesses, but because of the accurate histories there was little doubt as to the original source of infection.

In its early stages it is not always easy to diagnose the condition. Not only may there be some doubt as to whether the infection about the diaphragm is above or below that structure, but the decisions as to whether the infection will subside without suppuration and as to which of the spaces it involves are both of prime practical importance. Granted the case in which it is reasonable to suspect the presence of a subphrenic abscess, the diagnosis is made on one or more of the following points: the presence of tenderness over the twelfth rib or lower costal margin to firm palpation or compression; the clinical findings of a high, fixed diaphragm on the affected side, together with such manifestations of diaphragmatic irritation as pain referred to the shoulder or neck, hiccoughs and discomfort on deep respiration; and the confirmation by roentgenological studies of the clinical impression as to the position and excursion of the diaphragm.

TABLE 3. *X-Ray Data in 83 Cases* of Subphrenic Abscess.*

X-Ray Data	No. of Cases	Percentage of Total Cases
Diaphragm elevated	65	78
Diaphragm not elevated	3	4
Diaphragm not visualized	15	18
Fluid level and gas below diaphragm	22†	26
Opaque injection into pre-existing sinus	5	6

*In 28 cases no preoperative x-ray films were taken.
†One of these cases showed no fluid level, although gas could be demonstrated.

Table 3 gives the x-ray findings in the 83 cases so studied, and substantiates the statement of LeWald[7] that, regardless of the space involved, the

diaphragm if it can be visualized by x-ray will almost invariably be found to be elevated and usually fixed. The presence of gas and a fluid level occurred in 26 per cent of our cases, either as a late finding, or because of the introduction of gas into the involved area from a perforated viscus or an externally draining sinus. It should be remembered that following laparotomy alone, free air beneath the diaphragm may be demonstrated frequently by x-ray for as long as two weeks after operation, as brought out by Muller, Overholt and Pendergrass.[8] Those cases in this series in which no x-ray films were taken were largely the ones dating back to the earlier period when such studies were not readily available. In 5 of the cases, the

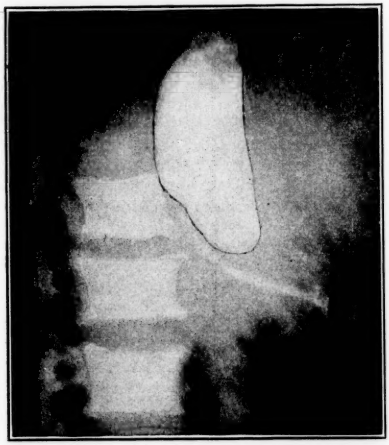

FIGURE 4. *Lateral X-Ray Film of an Abscess Cavity.*

This lies in the right posterosuperior space and has been injected with Lipiodol through a persistent sinus following cholecystectomy with drainage. There is some distortion due to the angle at which the exposure was made. The involved area has been retouched for greater clarity in the reproduction. The patient promptly recovered following drainage by the retroperitoneal type of approach.

injection of a radio-opaque substance into a sinus tract, persisting from previous operative drainage, served as a simple method of demonstrating the location of a residual subphrenic abscess (Fig. 4).

It is obvious from a review of the more recent records that in many cases the surgeon did not fully avail himself of the help that x-ray studies might have afforded, but was satisfied with a simple anteroposterior view and a statement that the diaphragm was elevated and fixed. There are, of course, patients so ill that it may seem unwise to attempt to secure a satisfactory lateral plate or to carry out fluoroscopic studies, but whenever the patient's condition will permit these procedures, the evidence so secured will be of inestimable help in establishing which of the subdivisions is involved.

The presence of serous effusion above the diaphragm is another suggestive sign of the existence of a subphrenic abscess, although opinions differ as to the constancy of this finding. Thus, Clute[9] and Beye[10] believe that it is almost invariably present, whereas Ochsner[1, 3] contends that it is usually a late finding in neglected cases. In attempting to arrive at a conclusion on this point from the findings in this series (Table 4), it seemed unwise

TABLE 4. *Findings as Regards Pleural Effusion Associated with Subphrenic Abscess.*

CLINICAL DATA	NO. OF CASES	PERCENTAGE OF TOTAL CASES
No chest tap or operative comment on visualization of pleural cavity	73	66
Empyema at time of subphrenic drainage	9*	8
No fluid by chest tap (4) or by visualization (5)	9	8
Pleural effusion by chest tap (20) or visualization (0)	20†	18
Total	111	

*78 per cent of these were grossly neglected cases occurring prior to 1924.

†85 per cent of these involved one of the superior spaces.

to hazard a definite statement as to the presence or absence of chest fluid in the 73 cases in which neither a chest tap nor direct visualization of the pleural cavity had been carried out. In 9 neglected cases, all but 2 of which occurred prior to 1924, a definite diagnosis of empyema had been established at the time of the subphrenic drainage. Thus, there remained 29 patients with subphrenic abscesses confirmed by operation whose pleural cavities were either explored by thoracentesis (24 cases) or by visualization at the first stage of the transpleural technic of subdiaphragmatic drainage (5 cases). Judged by such criteria, 8 per cent of the total number of cases showed no fluid, whereas 18 per cent showed it to be present in varying amounts.

It might be assumed that the longer the subphrenic abscess has been present without adequate drainage, the greater would be the incidence of pleural effusion. I fully realize that it is impossible to draw any final conclusions from these figures, but the fact that the average elapsed time between the onset of the original septic process and the exploration of the pleural cavity was thirty days in the cases in which no fluid was demonstrated, and twenty-six days in the ones in which an effusion was found, suggests that the duration of the subphrenic abscess is not the sole factor in

determining the incidence of pleural involvement.

The fact that 85 per cent of those cases in which the presence of fluid above the diaphragm was established had a subphrenic process involving one of the superior spaces, bears out the assumption that the abscess must almost always be in direct contact with the diaphragm in order to give pleural effusion above it.

Downward displacement of the liver is often difficult to determine, but if this finding can be established it is an added factor suggestive of an abscess in one of the superior spaces.

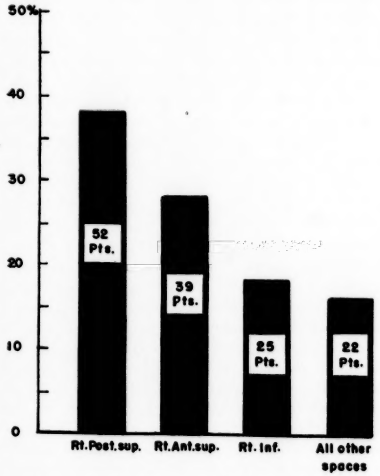

FIGURE 5. *Localization of Subphrenic Abscess.*

A total of 138 spaces were involved in the 111 cases. The "all other spaces" included: left superior, 8 per cent; left anteroinferior, 5 per cent; and retroperitoneal, 3 per cent.

It is disappointing to note that, as time has gone on, there has been no appreciable decrease in the average interval of twenty-six days between the time of the antecedent laparotomy and the institution of drainage for the subphrenic abscess, when both of these were carried out at the same hospital entry. It might well be expected, and is certainly to be hoped, that in future, with more intelligent interpretation of the x-ray data and less reticence in accepting suggestive findings as an indication for surgery, operation will be instituted earlier. I am sure that an occasional negative exploration early in the period when a subphrenic abscess is suspected is far more desirable than procrastination carried to a degree that renders the presence and location of the abscess self-evident.

Localization of Abscess

In 87 per cent of the cases the abscesses were on the right side (Fig. 5), with the right posterosuperior space most frequently involved (38 per cent), and the right anterior (28 per cent) and the right inferior (18 per cent) spaces of lesser importance; 3 per cent of the abscesses on the right side were in the retroperitoneal areas. The necessity of determining before operation which space or combination of spaces is involved cannot be overemphasized; this determination can best be made by an observance of the following factors:

The *location of the point of maximum tenderness.* It is at times difficult to elicit convincing evidence from pressure over the twelfth rib posteriorly or the lower costal margin anteriorly in the early stages of development of an abscess. However, repeated examinations will eventually show tenderness to be present over an involved space in practically every case. Not infrequently deep pressure or compression of the lower chest wall will elicit this sign when it cannot be demonstrated by lighter forms of palpation.

The *x-ray findings,* especially those shown by fluoroscopy and lateral films, and those taken after the injection of a radio-opaque substance into a pre-existing inadequately draining sinus tract.

A *consideration of the original septic process,*

TABLE 5. *Influence of Etiology on Spaces Involved in Subphrenic Abscess.**

Etiologic Factor	No. of Cases	Cases with More Than One Space Involved	Spaces Involved: Right Postero-superior		Right Antero-superior		Right Inferior		Left Side and Retroperitoneal	
			No.	Per Cent	No.	Per Cent	No.	Per Cent	No.	Per Cent
Appendix	35	10	24	48	9	18	10	20	7	14
Stomach and duodenum	30	5	9	29	12	39	5	16	5	16
Liver and bile passages	23	4	7	25	13	46	5	18	3	11
All other causes	23	5	12	41	5	17	5	17	7	25

*A total of 138 spaces were involved in the 111 cases.

with special reference to the most likely site of its extension beneath the diaphragm (Table 5). Thus, in the 35 cases in which an acute appendix was the causative factor, 68 per cent of the associated subphrenic abscesses were found in either the right posterosuperior or right inferior space. It is of interest to note that nearly half the abscesses following surgery on the gall bladder occurred not in the dependent right inferior space, which presumably was adequately drained at the time of operation, but in the contaminated but undrained right anterosuperior space. When the stomach or duodenum, either from perforation or previous surgery, was the source of the original infection, the right anterosuperior space was involved in 39 per cent of the subsequent subphrenic abscesses, and the right posterosuperior space in 29 per cent. More than one of the spaces was involved in 24 cases, the commonest combination of the right posterosuperior and right inferior spaces being found in 13 per cent of the series.

The *aspiration of pus from a suspected area* beneath the diaphragm. This adjunct to localization is mentioned here because of the frequency with which it is employed rather than because of any inherent merit in the procedure. Personally, I agree with Whipple,[11] Schwartz[12] and numerous others that it is a pernicious practice that should be condemned, because of the risk attendant on the removing of a contaminated needle through an uninvolved serous cavity. Although a productive tap is indisputable evidence of the presence of pus, failure to locate pus with a needle cannot be taken as evidence that no abscess exists, and the contention that because of the septic process beneath the diaphragm the lower portion of the pleural cavity will have become shut off by adhesions, making thoracentesis a perfectly safe procedure, cannot be relied on. The only time when I believe aspiration is justified is at operation after the preliminary steps have been taken so that the surgeon by direct visualization can satisfy himself that there is no possibility of contaminating an uninvolved area. Even under such circumstances an incision to permit a more generous exploration beneath the diaphragm would usually seem more desirable than the blind searching of the region with a needle. Attempts to locate the abscess by aspiration before operation are recorded in 13 cases, while an exploratory needle was used at the time of operation in 28.

Thoracentesis of the pleural cavity to determine the presence and nature of fluid in this space may be carried out to advantage in certain cases of suspected subphrenic abscesses in order to differentiate an empyema and a sterile collection of transudate above the diaphragm. However in such exploratory preoperative aspirations care should be taken that the tip of the needle does not pass beyond the confines of the pleural cavity.

Treatment

Granted the diagnosis of a collection of pus beneath the diaphragm, there is complete unanimity of opinion that the treatment lies in prompt drainage of the area. It is not within the province of this paper to give a detailed description of the various technics that may be employed, for any surgeon interested in the subject is already familiar with the transthoracic methods and the retroperitoneal types of approach. The moot question, however, of the choice between these two broad classifications of drainage is most pertinent. All surgeons would be in accord in favoring that procedure which will most promptly and effectively drain the abscess with the smallest risk to the patient. The final decision should be based on a consideration of fundamental surgical principles and a study of the reports contrasting the two methods of approach.

The advocates of the transthoracic approach argue that it is superior because it affords more direct access to the involved area. I believe, however, that they discount too readily the increased risk of contamination of the pleural cavity inherent in this type of drainage. The contention that such contamination will rarely occur seems to be controverted by the fact that soiling of the pleural cavity took place in 32 per cent of the cases so drained, the percentage being slightly higher if only the cases done in two stages be considered. The delay that a two-stage procedure necessitates is a further but less important consideration that is often overlooked.

It should be pointed out that in only 13 of the 42 cases drained by the transthoracic approach was the procedure done in two stages, for most of the earlier cases were done at a single operation. At the present time, few surgeons would defend the one-stage procedure save in exceptional cases, for it cannot be assumed that the pleural cavity at the costophrenic angle will have become obliterated because of the infectious process below the diaphragm. It is apparent from a study of the relatively small segregated group of cases done in two stages that the results are distinctly more favorable than would appear from the figures of this transpleural group as a whole.

The advocates of the retroperitoneal type of approach, so well described and illustrated by Ochsner and Graves,[3] contend that this method at a single operative step gives the abscess adequate dependent drainage with the smallest chance of contaminating uninvolved surfaces. In only 4 per cent of our cases in which this method was employed was either the pleural or peritoneal cavity

inadvertently opened and contaminated. The average postoperative stay in the surviving cases since 1917, when our convalescent home was abandoned, was forty-three days for the cases drained retroperitoneally, and fifty-eight days for those drained by the thoracic approach. Such a protracted convalescence, regardless of the type of operation employed, should not be necessary with prompter diagnosis and earlier institution of drainage.

In the cases in which the right posterosuperior or right inferior space was involved, the operative technic consisted of resection of the entire twelfth rib and division of the underlying fibers of the diaphragm and fascia in order to permit access to

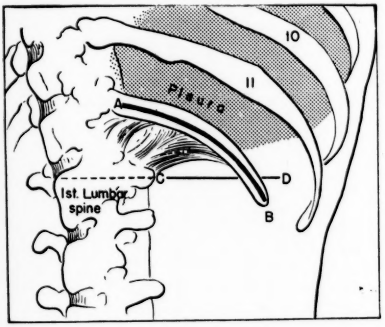

FIGURE 6. *Diagrammatic Sketch.*

This shows the proper line of division of the fascia (C–D) *at the level of the first lumbar vertebra. Such an incision invariably avoids contamination of the pleural cavity which would occur in certain cases if the dissection were carried down beneath the line of the skin incision* (A–B) *and through the bed of the twelfth rib.*

the retroperitoneal space. From this point, the abscess cavity could be reached by blunt dissection of the peritoneum and entered directly. In dividing the fascia, care should be taken to make the incision horizontally at a level of the first lumbar spinous process rather than obliquely along the bed of the twelfth rib (Fig. 6), as failure to observe this precaution will result in a disastrous contamination of the pleural cavity in a certain number of cases. This has been shown to be possible by Melnikoff[13] in a study of cadavers in which he demonstrated that the pleura on the right extends to below the twelfth rib in 62 per cent of all cases, but is never found as low as the level of the first lumbar spinous process.

In the retroperitoneal approach to the other subdiaphragmatic spaces, the incision was appropriately placed below the costal margin of the area in which tenderness could be elicited. Thus, in the right anterior space it was made obliquely below the ribs anteriorly and extended down to, but not through, the peritoneum. By blunt dissection, chiefly with the finger, the peritoneum was then separated from the overlying layers until the abscess cavity was reached and could be broken into without contamination of the general peritoneal cavity. The retroperitoneal type of drainage was employed in 49 cases.

There is no justifiable defense for the transperitoneal approach in the drainage of the superior subphrenic spaces, as it has no valid advantage over the other methods, and implies contamination of the peritoneal cavity. It is true that with the less commonly involved left inferior space this type of approach must necessarily be used. However, the formation of adhesions between the anterior abdominal wall and the underlying abscess in this group of cases usually renders the operation under these circumstances extraperitoneal, in the sense that there is no further contamination of the general peritoneal cavity. In the great bulk of the 20 cases done by the transperitoneal approach, this was carried out in the early years of the series, before the advantages of the retroperitoneal type of operation were fully appreciated.

MORTALITY RATE

It is hard to arrive at a fair criterion for determining the mortality rate attributable to subphrenic abscesses, because of the difficulty in evaluating the importance of the original focus of infection as a factor in a fatal outcome. Certainly many of these cases, even if they had never developed a subdiaphragmatic process, had ample cause for death, but to attempt to segregate the cases in which the fatality was due to the primary lesion from those in which the subphrenic abscess could be held responsible would introduce so large a variable human factor as to make the figures meaningless. For this reason, all the deaths in this series are included in computing the mortality rate of 37 per cent for the 111 cases as a whole.

Complications attributable to the fact that the subphrenic process arose prior to drainage or as a result of it contributed toward increasing the number of deaths. Delay in diagnosis was responsible in practically every case for the more serious complications present before operation. The occurrence, relatively early in the series, of 6 cases of rupture of the diaphragm, 3 of these resulting in bronchopleural fistulas, and of an additional 3 cases of pre-existing empyema brings out the dangers of procrastination.

That contamination of the pleural or peritoneal cavity at the time of operation will result in raising the mortality rate should be self-evident, and Table 6 bears out most strikingly the truth of this statement, for it will be seen that with soiling of either of these cavities there is well over a two-fold increase in the mortality figure. That there is a wide variation in the risk of such contamination with the different types of operation has already been referred to, and I believe that it is this factor which accounts for a difference in the mortality figures (Fig. 7) of 55 per cent for the transperitoneal approach, 41 per cent for the transpleural type of drainage and 27 per cent for the retroperitoneal operation. In the series of collected and personal cases reported by Ochsner,[1] the same relation existed and was even more striking, for in those cases the mortality rate in the patients drained by the retroperitoneal method was only slightly more than half that found with either the transpleural or the transperitoneal approach.

TABLE 6. *Effect of Contamination at Time of Operation on the Mortality Rate.*

LOCATION OF CONTAMINATION	NO. OF CASES	MORTALITY %
Both pleural and peritoneal cavities contaminated	1	100
Pleural cavity contaminated	16	69
Peritoneal cavity contaminated	17	53
Neither cavity contaminated	77	23
Total	111	
Grand average		37

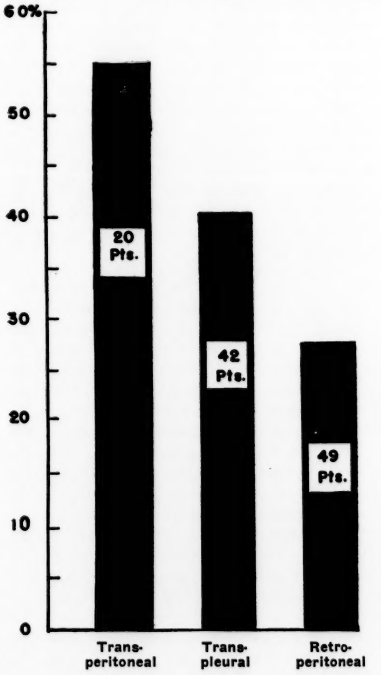

FIGURE 7. *Mortality Rate According to the Type of Operation.*

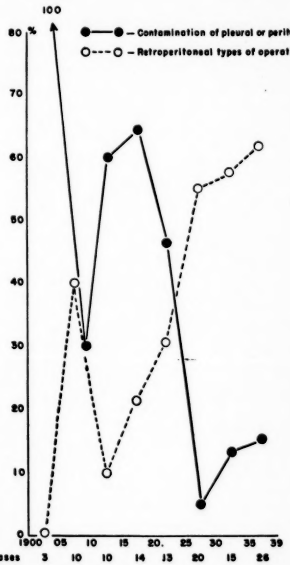

FIGURE 8. *The Percentage Contamination of the Pleural or Peritoneal Cavity and the Incidence of the Retroperitoneal Types of Operation, According to Five-Year Periods.*

A growing conviction that the extraserous approach is the safest type of operation accounts for our increasing use of this procedure (Fig. 8), and from a study of the cases it appears valid to conclude that the consequent proportionate decrease in the number of cases of contamination of the pleural and peritoneal cavities was due almost wholly to the wider adoption of the retroperitoneal operation. If Figure 8 be studied in conjunction with Figure 9, it will be seen that almost without exception the mortality rate has varied proportionately with the incidence in the use of the retroperitoneal type of operation.

It might seem from the above and from the published reports of others[1–3] that there would no longer be any sustained effort to defend the transpleural method of approach; yet in numerous recent cases I have found ardent champions of this apparently less desirable type of operation.

Summary and Conclusions

The statistical data relative to the 111 consecutive, drained cases of subphrenic abscess occurring at the Massachusetts General Hospital from 1900 to 1939 are presented. The importance of early and accurately localized diagnosis of the involved area is stressed. The advantages of the retroperitoneal over other surgical types of drainage are emphasized.

From these data it can be concluded:

At least one fifth of all infections in the subphrenic region subside without abscess formation.

The proper treatment of a subphrenic abscess is prompt surgical drainage.

A diagnosis of an abscess beneath the diaphragm that does not differentiate between which of the clearly demarcated subphrenic spaces is involved leads to hesitancy in the method and time of operation.

The right side is involved nearly seven times as frequently as the left, with the right posterior and anterosuperior spaces the site of the abscess in two thirds of all cases.

Contamination of the pleural or peritoneal cavities at the time of operation more than doubles the mortality rate.

Contamination of the pleural or peritoneal cavities occurs far more frequently with the transthoracic and transperitoneal types of approach than it does with the retroperitoneal operation.

Both the theoretical and the statistical evidence favor the retroperitoneal type of operation as the procedure of choice in the drainage of a subphrenic abscess.

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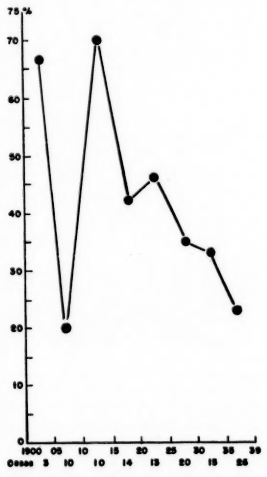

Figure 9. *The Mortality Rates According to Five-Year Periods.*

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Discussion

Dr. Howard M. Clute, Boston: In the consideration of subphrenic abscess, the first requirement, as Dr. Faxon has clearly pointed out, is the early recognition of the condition. He has shown very clearly that the patients who had had the disease for a long time were poor risks and had a poor chance of recovery.

In our hospital, when a postoperative case develops a fever, we expect that in the majority of cases, if we are careful enough and hunt hard enough, we shall find that the cause is in the abdominal wound. If we do not find it there we expect to find it in the pouch of Douglas, and if we fail to find it there, we take x-ray films of the chest in order to see whether or not a subphrenic abscess is present.

I think it is most important to point out that there are no pathognomonic symptoms — merely fever of unexplained origin coming on after operation or peritoneal trauma. That there is a possible etiology for subphrenic abscess in such a case should make us hunt actively for an abscess. If we do that we shall find it much more often, I believe, than any of us suspect.

Dr. Faxon pointed out that some 25 per cent of his

cases had evidence of definite subphrenic infection, which, however, did not go on to abscess formation. This shows how carefully he and his confrères follow these cases and points to the need for some delay before operating on early cases.

When I first became interested in subphrenic abscesses, the one-stage retroperitoneal approach, which Ochsner describes and Dr. Faxon and his associates advise, was not in common use and we were not familiar with it. We started with the two-stage transpleural method. I still use it, but I feel a little less in favor of it at the present time in view of Dr. Faxon's figures, and because of the obvious good sense of the one-stage retroperitoneal approach. We have, however, had very satisfactory results with the two-stage approach.

If you look at the ordinary picture that shows the relation of the parietal and diaphragmatic pleura, they appear to be widely separated. In cases of subphrenic abscess, however, the diaphragm is raised very markedly and the costophrenic angle is reduced or obliterated, and my experience has been that the diaphragmatic pleura and the parietal pleura are usually in close approximation.

Dr. Faxon has emphasized, and I agree, that the great danger in draining a subphrenic abscess is that you will give the patient additional trouble by soiling the pleural cavity and causing empyema. With this in mind, I have found it a good plan to remove 11 cm. or more of the tenth rib in the midaxillary or postaxillary line, suture the diaphragm to the parietal pleura and pack the wound. After twenty-four or forty-eight hours the pleural cavity is walled off. At the second operation there is afforded a large exposure, and one may enter the subphrenic area with freedom and ease and explore it. There should never be postoperative empyema.

I have tried to approach these abscesses on the side by taking out a piece of the tenth or eleventh rib and pushing up the pleura, being careful not to perforate it. I think that this is a highly dangerous procedure, since it is very easy to make a small opening in the pleura. I have noted in Ochsner's article — and I believe Dr. Faxon also says so — that even in the retroperitoneal approach the pleura runs to the level of the twelfth rib and sometimes a little beyond, a place where it is apt to be injured. I am inclined to think that the transpleural approach has advantages, chiefly because the surgeon recognizes that the pleural cavity is in danger and takes care to wall it off, and because there is a large exposure for the second stage, thus facilitating exploration of the subphrenic area and drainage of the abscess.

Dr. Thacher W. Worthen, Hartford, Connecticut: This is a timely subject, and I agree with Dr. Faxon's conclusions. Analyzing the figures in his series, one arrives at the fact that the yearly average incidence was between 4 and 5 cases. If one eliminates the cases with the diagnosis of subdiaphragmatic inflammation which were not confirmed either by operation or by autopsy, the incidence was only about 3. A series of cases at the Hartford Hospital, covering a ten-year period, had nearly the same incidence. The mortality in this group was a little over 20 per cent.

The real problem that the review of these cases revealed was the difficulty of finding the abscess at operation. Three cases were diagnosed at autopsy as subdiaphragmatic abscess, but no pus had been found at operation. In 2 of these cases an anterior and a posterior approach had been made; yet a large collection of pus in the posterosuperior space had not been found.

The surgical treatment of subdiaphragmatic abscess may be approached from two points of view, the conservative and the radical. A certain degree of conservatism is warranted in some cases in the early stages of the formation of the abscess, because there are cases of so-called subdiaphragmatic inflammation which do subside and for which surgical interference may be unnecessary. Perhaps it is not wholly accurate to call them abscesses in this stage. On the other hand, in the presence of a positive diagnosis of subphrenic abscess, early interference by the extraserous approach, either anterior or posterior, seems the logical one. Dr. Clute's success with the transpleural approach speaks for itself, however, and has given him excellent results. I cannot help but feel that Dr. Faxon has made a real contribution to the subject.

Dr. Torr W. Harmer, Boston: This subject is interesting from its anatomical basis, and from the nicety of the Nather-Ochsner operation. In order to appreciate the adult anatomic relations it is necessary to consider the embryology, and to think of the liver as developing between the leaves of the anterior mesentery, which extends to the umbilicus with the umbilical vein in its free margin, and of the early attachment of the liver to the diaphragm posteriorly. Dr. Faxon spoke of the high attachment on the right side. If one follows the peritoneum up the anterior parietes onto the undersurface of the diaphragm, it becomes reflected onto the front face of the liver at the anterior margin of its attachment. If one ascends the posterior parietes, it passes over the right suprarenal gland and then onto the undersurface of the liver. These reflections onto the liver form the two leaves of the coronary ligament.

I think that with this embryological concept one can appreciate the anatomical situation. It is also interesting to do the Nather-Ochsner operation on cadavers; having performed this operation many times with medical students over a period of years, I am impressed with its anatomical nicety.

My own experience since Nather and Ochsner published their contribution in 1923 is meager. I have had only 6 cases; 2 were seen very late, the patients having scaphoid abdomens and being practically "skin and bone." One abscess was in the left posterior space, one in the right anterior space and four in the right posterior space. There were 2 fatalities; in one the abscess was in the right anterior space, and in the other it was in the right posterior space.

One thing which Dr. Faxon mentioned but which is worth emphasizing is the fixity of the diaphragm on fluoroscopic examination. I had this impressed upon me by a case in which the diaphragm was pushed up but not fixed. There proved to be a solitary abscess of the liver about 8 cm. in diameter, and not a subphrenic abscess as I had at first thought. The fluoroscopic examination was repeated, and the radiologist still made a diagnosis of subphrenic abscess. I explored anteriorly and drained the abscess, with a successful outcome.

Dr. Irving J. Walker, Boston: It seems to me that if right-sided subdiaphragmatic abscesses are difficult to diagnose, those on the left are even more so, at least in my experience. I wish to comment on 9 cases seen by me during the last four years. All these occurred following general peritonitis secondary to acute appendicitis. The story in each was similar: that of a patient who had had peritonitis associated with appendicitis. A pelvic abscess was drained in each case. This was followed by a persistent temperature which could not be accounted for.

Naturally we investigated the chest, the right subdiaphragmatic region, and finally, but usually rather late,

the left. While this study was going on the patient would have a slight cough and complain of some very indefinite low-grade pain in the left upper quadrant. The medical consultants usually said that there were rales at the left base consistent with atelectasis. Of course the latter existed, but, as later events showed, it was due to a lesion below the diaphragm. Palpation showed slight tenderness below the left costal border.

X-ray examination done early in the course of the disease usually showed a pneumonic process at the left base. The surgeon, not being entirely satisfied, would naturally reason that perhaps after all there was a lesion beneath the diaphragm. The diaphragms were not elevated in all cases, which did not rule out the possibility that there might be some lesion beneath them. It would seem to me that the important point of the x-ray examination lies in the fact that when the patient was examined under the fluoroscope it was found that the left diaphragm either was fixed or moved only slightly. I therefore lay greater stress on fixation of the diaphragm than I do on its elevation, since fixation occurred in all our cases. Of these 9 cases 8 were discovered and operated on. The ninth was not found until postmortem examination.

Our surgical approach in these cases was transperitoneal. We reasoned that these abscesses occurred as a result of unrecognized pelvic abscesses, or abscesses of the pelvis which had been allowed to remain undrained for too long a period of time, the result being slow seepage from the abscess up the gutter along the outer side of the sigmoid and descending colon, and finally an accumulation of pus under the left diaphragm. We justified our transperitoneal approach because of the fact that our incision would give dependent drainage, and that the peritoneal cavity would probably not again become infected, since it was already immune to the same infection as that which produced the subdiaphragmatic abscess.

All these cases were drained by an incision under the left costal border. We early found that it was necessary to use a large tube or two smaller tubes for drainage, and that we should not remove these tubes too early, otherwise we would have a cavity under the diaphragm with a bottle-necked sinus which would be insufficient to drain the abscess. From time to time we injected the cavity with Lipiodol, gradually removing the tubes and omitting them entirely when the sinus was very small. All the 8 patients who were operated on recovered.

Dr. Faxon (closing): Apropos of what Dr. Clute has said in regard to possible damage to the pleura in the retroperitoneal type of operation, I should like again to stress the points brought out in Figure 6. From the studies of Melnikoff, the pleural cavity never extends as low as the level of the first lumbar spine. This being the case, no contamination of the cavity can occur if the fascia be incised along the *C–D* rather than the line of skin incision and bed of the twelfth rib, *A–B*.

Another advantage of the retroperitoneal approach that I did not mention is the fact that with this operation both the right posterosuperior and right inferior spaces are equally accessible for drainage, whereas with the transthoracic approach such latitude of exploration is impossible.

If the anterior spaces are to be drained, care should be taken that the incision along the lower costal margin goes to, but not through, the peritoneum. By blunt dissection the abscess can then be readily reached without entering the general peritoneal cavity.

I agree that it is most important that a sufficiently large opening be instituted and maintained in order to avoid a bottle-neck type of abscess and premature blocking of drainage.

HEBERDEN'S NODES: THE INCIDENCE OF HYPERTROPHIC ARTHRITIS OF THE FINGERS*

ROBERT M. STECHER, M.D.†

CLEVELAND

HEBERDEN'S nodes are enlargements of the terminal interphalangeal joints of the fingers. Little detailed information concerning these enlargements is available, although they are mentioned frequently in the medical literature. They have been variously ascribed to gout and to rheumatoid arthritis, but it is the consensus that they are due to hypertrophic arthritis. This particular form of hypertrophic arthritis lends itself readily to statistical analysis because it constitutes a clear-cut clinical entity, the diagnosis can be made with reasonable certainty by looking at the fingers, the degree of involvement can be estimated quantitatively, and the disease is relatively common.

Most studies on the incidence of arthritis have been devoted to determining the proportion of the population disabled by rheumatic diseases.[1] Such investigations are of importance from the social, economic and public-health standpoints, but yield little or no information concerning the causes or nature of any particular disability.

The present study is an attempt to evaluate the influence of age, sex, race and occupation on the incidence of Heberden's nodes. It is undertaken with the hope that exact information concerning this particular form of hypertrophic arthritis will reveal characteristics which might not be apparent from studies of the disease in general.

LITERATURE

The syndrome derives its name from Heberden,[2] who first described it in 1802 as "digitorum nodi." His description is so short as to warrant quotation in full. He wrote:

> What are those little hard knobs, about the size of a small pea, which are frequently seen upon the fingers, particularly a little below the top, near the joint? They have no connection with the gout, being found in persons who never had it: they continue for life: and being hardly ever attended with pain, or disposed to become sore, are rather unsightly than inconvenient, though they must be some little hindrance to the free use of the fingers.

Charcot[3] gave a more complete and detailed description of the clinical and pathological characteristics of the disease, based on personal observation. He added that the end of the finger is often bent a little to the right or left. Usually the onset is very obscure; however, there are attacks of redness, heat and temporary swelling of the soft parts, really exacerbations of the affection which the patients often regard as paroxysms of gout. "These nodosities are interesting to the observer," he said, "because they reveal a constitutional state which is none other than the rheumatic diathesis." Charcot noted that Heberden's nodes belong especially to old age but may be seen in young people; that the disease is hereditary; and that it occurs with partial rheumatism (hypertrophic arthritis). He stated that Heberden's nodes are often accompanied by asthma, migraine, neuralgia and muscular rheumatism, and that they are commonly seen in patients with cancer of the breast.

Duckworth[4] mentioned that the disease is seen in people of advanced age, and agreed with Charcot that cancers of the breast and uterus are not infrequently associated with it. "When occurring in men without any pronounced gouty or rheumatic concomitant," he wrote, "they may support a general prognosis for longevity." He cited a case in which Heberden's nodes occurred in three generations. Duckworth quoted Begbie to the effect that they are seldom or never seen in the fingers of the industrious laborer or hard-working mechanic, but are found chiefly among the upper classes or the luxurious and well-fed or their dependents.

McCrae[5] asserted that Heberden's nodes are commoner in advanced years but may occur in younger people. He mentioned a sixteen-year-old boy with large nodes occurring as part of a generalized arthritis. In another patient, a woman thirty-two years of age, the nodes developed rapidly in all the fingers. They may occur as the only manifestation of arthritis. McCrae mentioned the irregular distribution, the usual lack of serious symptoms and the deflection and deviation often seen in the terminal phalanges.

PATHOLOGY

The pathologic changes found in Heberden's nodes have been described by numerous observers. Charcot[3] gave an excellent account of these changes. He said:

> The articular cartilages undergo the velvety change: then they disappear, and an eburnated osseous layer

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is found in their place. The articular surfaces enlarge in all directions on account of the growth of osteophytes, which almost exactly reproduce in an exaggerated form their shape and natural contours. There is no trace of sodium urate deposits, either in the substance of the articular cartilage or in the soft part in the neighborhood of the joints.

Nichols and Richardson[6] in 1909 asserted that Heberden's nodes were due to degenerative (hypertrophic) arthritis. Their description of the changes in the cartilage found in degenerative arthritis is quite similar to that given by Charcot. They stated that the changes consisted in an increase in the activity of the perichondrium, resulting in the new formation of cartilage which might be transformed into bone.

Brogsitter[7] examined histologically the nodes of 17 fingers. He found the characteristic changes of hypertrophic arthritis, namely irregular erosion and fibrillation of cartilage, cystic and fibrotic areas in the hyperemic bone marrow, and spur formation. The most interesting findings, however, were in the small blood vessels. These lesions consisted of typical arteriosclerotic changes with narrowing of the lumen by intimal proliferation, and even complete occlusion of the vessels with old and canalized thrombi. The media was infiltrated with round cells, in places to a sufficient degree to lead to rupture of the vessels and hemorrhage into the surrounding tissue. Because of these findings Brogsitter believed that Heberden's nodes occurred as a result of decreased circulation in the bone and disturbance in nutrition of the joint cartilage. He found uric acid tophi in 3 of the 17 fingers examined, but thought that Heberden's nodes in general were due to hypertrophic arthritis.

Stockman[8] concluded that Heberden's nodes were not a manifestation of osteoarthritis because he "examined a number of specimens all of old standing and did not see the peculiar changes characteristic of true osteoarthritis. In all the joint had remained intact, and the cartilage was normal in appearance."

Etiology

Before Heberden's time, nodules on the fingers were considered to be typical manifestations of gout. Heberden[2] did not know their cause but disagreed heartily with the conventional view of the time. Charcot[3] believed they were a special form of chronic rheumatism having nothing to do with gout. Garrod[9] stated that Heberden's nodes might be regarded as constituting the slightest and most chronic manifestations of rheumatoid arthritis, and that "their formation appears to be of the nature of a senile change." He employed the term "rheumatoid arthritis" to include chronic arthritis of all types. Duckworth[4] thought that some cases of Heberden's nodes were due to gout, and quoted Begbie, who was convinced of the occasional gouty nature of the disease. Brogsitter[7] found uric acid tophi in 3 of the 17 nodes examined, but thought that the nodes in general were due to hypertrophic arthritis. Stockman[8] did not commit himself as to their true nature except to doubt that they were caused by hypertrophic arthritis. McCrae[5] mentioned their occurrence in gouty patients but believed them to be usually a manifestation of arthritis deformans. Fox and Van Breeman[10] regard the condition as a form of gout modified by sex.

Cecil[11] states that Heberden's nodes are a form of hypertrophic arthritis but that the cause is not known. He is convinced that they are related in some way to repeated trauma because they occur most frequently in people who use their hands continually. Cecil does not mention the menopause as a cause of Heberden's nodes, but says that the diagnosis of menopausal arthritis is justified if on examination there is crepitation without swelling of the knees and Heberden's nodes of the fingers. Hench[12] believes that Heberden's nodes are a form of hypertrophic arthritis. Concerning the influence of trauma he writes, "Heberden's nodes are seen no more frequently, indeed perhaps less frequently, in elderly typists and needleworkers than in congenital dowagers, contrary to expectation if trauma was a prime cause." Dawson[13] states that the nodes constitute one of the commonest of all forms of osteoarthritis, and most commentators[3–5, 7, 10–12, 14–21] agree that they are typical manifestations of hypertrophic or osteoarthritis.

Plan of Study

This study was undertaken in order to determine the incidence of Heberden's nodes in the general population, analyzed according to race, sex, age and occupation. It reveals the proportion of individuals having several degrees of involvement of Heberden's nodes at any one time in the various race, sex, age and occupational groups. In order to accomplish this object I have examined nearly 7000 adult subjects. Most of these people were seen on the wards or in the dispensaries of two public hospitals in Cleveland. Because of the scarcity of elderly patients in the dispensary and hospital population, the inmates of several homes for the aged were included. Efforts were made to employ random sampling and to avoid bias, so far as possible. Subjects were examined only in groups as in a dispensary waiting-room, a hospital ward or a section of an old folks' home, and every one of the group was included in the

tabulation. Isolated observations were excluded, since it was believed that such observation might bias the results because of the temptation to include occasional, affected individuals to the exclusion of normal subjects. My private patients also were excluded because of the high proportion of arthritic patients in this group.

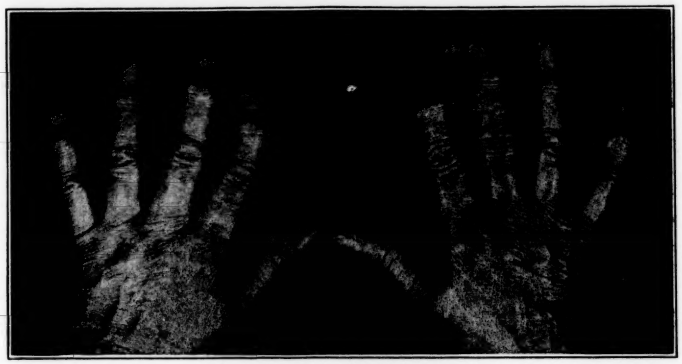

FIGURE 1. *Idiopathic Heberden's Nodes.*
The fourth fingers show only enlargement; the other fingers also show flexion deformity, and the index fingers, lateral deviation. The thumbs are not affected.

ease had been well and active until a few years before observation, and had therefore led a normal existence until quite recently. So far as Heberden's nodes are concerned, I believe that the subjects of this study represent a fair sampling of the working people of the moderate-income and low-income groups of Cleveland. For comparison with a different social and economic group the study includes a tabulation of over 500 physicians.

TABLE 1. *Analysis of 6913 Subjects Examined for Heberden's Nodes, Classified as to Race, Sex, Age and Occupation.*

CLASSIFICATION	NO. OF SUBJECTS IN DIFFERENT AGE GROUPS							
	10–19	20–29	30–39	40–49	50–59	60–69	70–79	80–89	90+
2233 white men (hospital population):									
Total subjects	115	324	306	446	439	353	203	44	3
Affected subjects	2	28	27	51	84	101	65	13	2
2187 white women (hospital population):									
Total subjects		500	498	512	306	207	125	34	5
Affected subjects		1	18	34	47	57	51	12	3
846 Negro men:									
Total subjects		184	249	191	131	75	16		
Affected subjects		16	16	20	17	16	3		
1117 Negro women:									
Total subjects		330	346	255	124	48	12	2	
Affected subjects		0	9	7	5	8	3	1	
530 white physicians:									
Total subjects		104	147	165	73	34	7		
Affected subjects		2	7	8	10	5	1		

The fact that the group observed was composed of the hospital population and not of normal individuals does not impose any serious inaccuracy for the purposes of the present study, for none of these people sought hospital care because of Heberden's nodes. Most of the patients were in good health except for some minor or acute illness which had no bearing on the presence or absence of the nodes. Even those with chronic dis-

TECHNIC

Notations were made on a separate card for each subject, the name, race, sex, age and the abnormalities of each finger being recorded. The positive and negative cards were separated, and each of these groups was then sorted as to race, sex and

age by decade. The cards were filed alphabetically in the proper classification. When a subject was seen for the second time, this card was found upon filing to be a duplicate and was discarded.

Three degrees of involvement of affected fingers were described by a simple system of notation. These are, in the order of increasing severity, as follows: enlarged; enlarged and flexed; enlarged, flexed and deviated. Enlargement of the joints sufficient to be visible and palpable was considered necessary for a diagnosis. This enlargement is occasionally apparent as two small nodules on the dorsolateral aspect of the terminal joint, but more frequently is noted as a definite ridge across the dorsum. At times enlargement is found to be soft or even fluctuant. When the disease occurs in a more advanced form, this enlargement extends to the lateral aspects of the joint also, and finally in extreme cases is evident by palpation on the palmar surface. As enlargement increases the bone deformity is associated with flexion of the terminal phalanx. In advanced stages the finger shows not only palmar flexion but also lateral deviation toward either the radial or the ulnar side. In rare cases there may be involvement of the proximal interphalangeal joint, evidenced by the presence of deformity, enlargement and limitation of motion.

The description thus far has concerned a single finger. Several fingers are often involved. The degree of involvement affecting the different fingers varies considerably, but rarely are all the fingers involved to an extreme degree. The thumbs seem to be comparatively immune, perhaps because there is no second interphalangeal joint of the thumb. Involvement of the toes has not been observed.

As experience accumulated during the progress of these observations it became apparent that Heberden's nodes developed in two different ways. Individuals with involvement of only one finger or of several fingers of the same hand usually attributed the deformity to a definite injury. Trauma resulted in swelling and pain, followed shortly by deformity that reached its final stage within a few months, after which no further change occurred. This condition has been designated as *traumatic* Heberden's nodes.

Individuals with the fingers of both hands deformed usually stated that the disease began with pain and swelling of one finger, that other fingers became successively involved, that deformity gradually increased and that the disease progressed for several years until the condition became stationary. In this group the changes seemed to arise spontaneously without reference to injury or associated disease, and the condition has therefore been designated as *idiopathic* Heberden's nodes.

For the purposes of statistical study, an arbitrary distinction has been made between the traumatic and idiopathic nodes. Subjects with involvement of less than flexion degree of one finger of each hand have been considered to have traumatic Heberden's nodes. Subjects, therefore, who had involvement at least to flexion degree of one finger of each hand were considered to have idiopathic Heberden's nodes. Inasmuch as histories were not obtained from these subjects (except for the information recorded on the card), an exact discrimination in individual cases was not possible. It must be emphasized that this differentiation into traumatic and idiopathic nodes is only ap-

TABLE 2. *Percentage Incidence of Heberden's Nodes Found in 6913 Subjects Classified as to Race, Sex, Age and Occupation.*

CLASSIFICATION	PERCENTAGE INCIDENCE IN DIFFERENT AGE GROUPS							
	10–19	20–29	30–39	40–49	50–59	60–69	70–79	80–89	90 +
2233 white men (hospital population):									
Total incidence	1.7	8.6	8.8	11.4	19.1	28.6	32.0	29.5	66.7
Traumatic nodes	1.7	7.1	8.0	9.2	15.5	23.2	23.6	11.4	33.3
Idiopathic nodes	0.0	1.5	1.0	2.2	3.6	5.4	8.4	18.2	33.4
2187 white women (hospital population):									
Total incidence		0.2	3.6	6.6	15.4	27.5	40.8	32.3	60.0
Traumatic nodes		0.2	3.2	5.7	12.7	12.1	16.8	5.9	0.0
Idiopathic nodes		0.0	0.4	1.0	2.6	15.5	24.7	29.4	60.0
846 Negro men:									
Total incidence		8.7	6.4	10.5	13.0	21.3	18.8		
Traumatic nodes		8.2	6.0	10.0	9.9	14.7	12.5		
Idiopathic nodes		0.5	0.4	0.5	3.1	6.7	6.3		
1117 Negro women:									
Total incidence		0.0	2.6	2.7	4.0	16.7	25.0	50.0	
Traumatic nodes		0.0	2.3	2.7	4.0	14.6	16.7	50.0	
Idiopathic nodes		0.0	0.3	0.0	0.0	2.1	8.3	0.0	
530 white physicians:									
Total incidence		1.9	4.8	4.8	13.7	14.7	14.3		
Traumatic nodes		1.9	4.8	4.8	11.0	11.8	14.3		
Idiopathic nodes		0.0	0.0	0.0	2.7	2.9	0.0		

proximate, but it serves a useful purpose in distinguishing degree of involvement, and reveals certain definite trends which seem significant.

Figure 1 illustrates the typical appearance of Heberden's nodes. The fourth fingers show only enlargement of the terminal joint. The other fingers show flexion deformity as well as enlargement. The index fingers show also lateral deviation of the terminal phalanges. The condition of any one of these fingers might have resulted from trauma. It is extremely unlikely that trauma affected all of them. The picture is one of idiopathic Heberden's nodes.

The observations upon which this study is based are presented in two tables and a chart. Table 1 shows the total and the affected subjects observed in the different race, sex, age and occupation groups. Table 2 presents the same material in percentage form. The total incidence and the incidences of traumatic and of idiopathic nodes are indicated for each subgroup. The information in Table 2 is presented in graphic form in Figure 2; because of the small number of persons, the white subjects over the age of eighty-nine and the colored subjects over seventy-nine have been omitted. The percentages in the last-mentioned

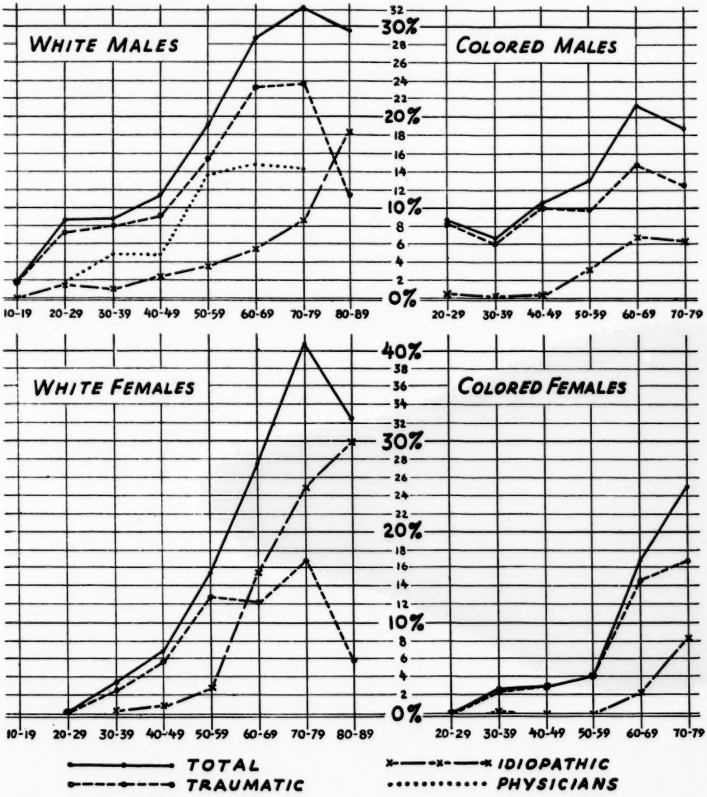

FIGURE 2. *The Percentage Incidence of Heberden's Nodes in 6913 Subjects, Classified as to Race, Sex, Age and Occupation.*

The total incidence has been subdivided into traumatic and idiopathic for all groups except physicians.

groups are completely out of line with the trend in the other classification. The group of physicians observed between the ages of seventy and seventy-nine was similarly small, but has been included because all the groups in the physicians are small and the last-named group conforms to the general trend. It will be seen that twenty-four of the thirty-six age groups shown in Table 1 include 100 or more individuals.

Discussion

Several possible sources of error in this study deserve mention. The problem of diagnosis in borderline cases is no different in this condition from what it is in any other disease. Inasmuch as the observations were all made by me, the same rules and the same criteria prevailed in all observations. Clubbing of the fingers is never a source of confusion. In this condition the enlargement is confined to the terminal phalanx, the enlargement is greater at the end of the phalanx than it is at the joint, and the fingernail is distinctly enlarged and rounded in both diameters. Two other conditions are more puzzling, and caused some difficulty in the beginning. One is flexion of the terminal phalanx without arthritis or enlargement of the joint, which occurs with rupture of the deep extensor tendon. Ability to extend the terminal phalanx is lost, but passive extension is full and complete. Deviation of the little finger occurring symmetrically as a hereditary trait is also without enlargement or arthritis of the joint. Certain sources of statistical error are worthy of comment. No note was made of missing fingers. Patients with one hand, 1 with claw hands and 1 with webbed fingers were omitted.

The age in every case was recorded as given by the subject. Many Negroes are uncertain as to their exact age and seem to be careless in their statements concerning it. It is thought that middle-aged white women are inclined to underestimate their age. These inaccuracies cause no practical difference and introduce only a slight statistical error. According to the system of tabulation used, no error whatsoever is introduced unless the age is given in the wrong decade. The classification according to race is social rather than anthropological.

Trauma

Trauma is a definite cause of many cases of Heberden's nodes, especially in subjects with involvement of one finger, or of several fingers of one hand. Inquiry recalled a specific injury, often accurately dated, directly involving the affected fingers. Such injury was followed by a painful swelling, leading in the course of several months to a painless deformity, which remained unchanged thereafter. Baseball injuries, such as a blow on the end of the finger by a fast ball, were predominant among younger men and boys, but were also described by older individuals. One subject with deformities of most of the fingers of the left hand said that he had been a left-handed catcher. Another subject, aged sixty-five, with deflection deformity of the right forefinger, had suffered a dislocation of that finger forty-five years previously when struck on the end of the finger by a fast-pitched ball. No change had been noted in this condition since the first few months after the accident. Several women with one enlarged finger attributed it to a baseball injury. Injuries received in other sports, such as football, basketball and skating, were followed by similar results. Industrial accidents played an important role. It was not uncommon to find cases of traumatic amputation with Heberden's nodes on the adjacent fingers.

The inclusion of traumatic arthritis of the terminal interphalangeal joints in the category of Heberden's nodes is justified. In this study any enlargement of these joints due to hypertrophic arthritis is considered as Heberden's nodes, and traumatic arthritis is considered to be hypertrophic arthritis. According to Doub,[22] traumatic arthritis has come to mean those chronic changes, such as synovial thickening, necrosis of the cartilage with narrowing of the joint space, and bone proliferation, which resemble arthritis and occur in and around a joint after injury. This arthritis simulates the type which goes by the name "hypertrophic" (osteoarthritis or arthritis deformans). Doub further states that traumatic arthritis must satisfy the following criteria: there must be proof of injury and of its severity; the injury must have been applied directly to the joint in question; information must be obtained as to the previous function of the joint in question; the time interval between injury and the occurrence of pathologic changes must be within the generally accepted limits (three to six months or perhaps a year); there must be clinical and roentgenologic evidence of pathologic tissue change. Doub quotes several authorities (Axhausen, Engelhardt and Blencke) who believe that injury must be severe enough to damage cartilage before traumatic arthritis ensues. Leriche,[23] on the other hand, believes that traumatic arthritis results from cartilage damage due to a hyperemic reaction following local traumatic shock. Allison and Ghormley[21] state that true traumatic arthritis is indistinguishable microscopically from degenerative arthritis. Traumatic Heberden's nodes conform to all the requirements of traumatic and therefore of hypertrophic arthritis.

The histories obtained from subjects with idiopathic nodes are in striking contrast to those obtained from subjects with traumatic nodes. In the former cases no history of injury can be elicited. The nodes arise spontaneously without coincident illness or recognizable predisposing cause. The affection of one finger is followed by involvement of more fingers one after the other for a period of months or years. In the beginning swelling may be soft or even fluctuant, there may be slight redness and tenderness, but these symptoms disappear when the final nonprogressive stage of the deformity is reached. The so-called wear and tear of everyday life has been blamed, especially in people who have worked hard, but this is an unsatisfactory explanation. The condition occurs in hard-working people, as this survey indicates, but severe Heberden's nodes are frequently encountered in women of the leisure class. Further consideration of the constitutional and environmental factors in the etiology of idiopathic Heberden's nodes will be discussed in another study. It should be noted that it is impossible to distinguish in a single joint between traumatic and idiopathic Heberden's nodes by clinical and roentgenological examination alone and without reference to the history.

The arbitrary classification into traumatic and idiopathic Heberden's nodes necessitated by inadequate history of the subjects of this inquiry leads to individual cases of error. Certain it is that some individuals develop nodes on the fingers of both hands as a result of trauma and are erroneously classified as having idiopathic nodes. Conversely, subjects developing idiopathic nodes are occasionally seen in a stage when only one finger or several fingers of the same hand are involved and are classified erroneously as having traumatic nodes. Such errors are in the opposite direction and tend to cancel the previous ones. A curious effect of what may be inaccuracy of classification is seen in the chart concerning white subjects. The incidence of idiopathic nodes increases gradually until a certain age,—seventy-nine for men, fifty-nine for women,—after which the incidence increases very rapidly. Coincident with this rapid rise of incidence of idiopathic nodes, the incidence of traumatic nodes falls. It seems possible that the apparent increase of traumatic nodes before this trend is altered may in reality be due to the development of idiopathic nodes which have not reached the stage at which they are recognized as such. Even though the arbitrary classification into traumatic and idiopathic types may introduce certain errors, the figures on the incidence of the different degrees of severity of Heberden's nodes are believed to be thoroughly reliable.

Age

Age is a definite factor affecting the incidence of Heberden's nodes, the incidence increasing as age advances. This is demonstrated for both idiopathic and traumatic nodes, regardless of sex, race or occupation. Heberden's nodes are seen in the third decade among all groups except Negro women. They are seen in the second decade in white men, the only group in which this age was investigated. Traumatic nodes are common in men, even at early ages, and are relatively rare in women. They increase with advancing years in almost every group, though the rate of increase is irregular and varies in different groups. Idiopathic nodes are rare at early ages; the incidence shows a gradual and regular increase with age. After the age of fifty-nine in white women and sixty-nine in white men and Negro women the increase is more rapid. Heberden's nodes are permanent deformities which, once developed, remain for life. The incidence is cumulative, and each new increment, as it occurs, is added to the increment already present. In any group of the population, the incidence will increase with advancing age so long as the factors causing them are operative.*

Sex

Sex is an important factor in determining the incidence of Heberden's nodes, in both white and Negro subjects. The incidence of traumatic nodes is higher in men than in women as early as the third decade, and increases at a higher rate throughout life. This difference can be attributed to environmental factors rather than to true sex differences. The educational, recreational and occupational activities of men differ considerably from those of women. The sports which they enjoy, baseball, football and basketball, are much more likely to produce finger injury than are those in which women usually indulge. In the shop, the fingers of many men are constantly exposed to industrial accidents. Men and women seem to be equally exposed to certain injuries in their homes and private lives which lead to Heberden's nodes, such as pinching of the fingers in doors and other minor household accidents.

Race

A comparison of the incidence of Heberden's

*Even in the face of these conditions, a decreasing incidence in advanced years is a theoretical possibility. Two conditions would be necessary. The presence of Heberden's nodes would have to be associated with an increased death rate to such an extent that these subjects would disappear faster than that part of the population which was free of Heberden's nodes, and faster than new cases developed. Such was not the case, however, among the subjects examined.

nodes in white and Negro subjects reveals certain differences. The gross incidence is higher in Whites. The difference is slight before the age of fifty, after which it becomes substantial. In men, this difference is almost entirely due to the markedly higher incidence of traumatic nodes in Whites. In women the incidence of traumatic nodes is essentially the same in both races except in the fifth and six decades, in which white women are affected respectively two and three times as frequently as Negro women. The incidence of idiopathic nodes in white and Negro males is essentially the same at all ages. Idiopathic nodes are rare in Negro women, in contrast to the high incidence found among white women. This is surprising in view of the fact that Negroes are more susceptible than are white people to the so-called degenerative diseases. The death rate from chronic nephritis, organic diseases of the heart, cerebral hemorrhage and other diseases of the arteries is distinctly higher among Negroes[24, 25] than it is among white people. Negroes are said to succumb to hypertensive heart disease on the average ten years earlier than do Whites. Despite the susceptibility of Negroes to disease of the small arteries, and the evidence that small artery disease is a factor in the production of Heberden's nodes, this condition is rare among Negroes.

Occupation

Occupational factors seem to affect the incidence of Heberden's nodes only in so far as they influence the hazard of finger injury. The gross incidence in physicians is distinctly low in all age groups. The incidence of traumatic nodes in physicians is one half or less in all age groups save the sixth decade, in which it reaches two thirds. The difference in the third decade is striking. It appears that this decade is specially hazardous for workingmen, so far as finger trauma is concerned. At this period of life physicians are in medical school, in hospital service or early practice. They have relatively little time for athletic sports, and they are "finger-conscious." The incidence of idiopathic nodes in physicians, while lower, appears to be approximately the same as that found in workingmen. This suggests that environmental factors, working conditions, housing, clothing, diet and other refinements of living are not important in the production of Heberden's nodes. The number of physicians observed in the upper age groups is so small as to cast considerable doubt on the reliability of the figures for idiopathic nodes.

General Considerations

Observations on a large number of individuals of various ages have revealed the incidence of Heberden's nodes. Similar results would be obtained by observing the incidence of Heberden's nodes as they occur at different ages in a large group of individuals who are examined repeatedly and periodically. From a statistical standpoint, and so far as Heberden's nodes are concerned, we may assume, for instance, that the white working males seen in the seventh decade present a picture similar to that which the white males of the third decade will show forty years later. We have, so far as Heberden's nodes are concerned, repeatedly observed the equivalent of five different groups, each numbering several hundred individuals, over a period of fifty or sixty years.

The probability of an individual's having hypertrophic arthritis of the fingers (Heberden's nodes) has been demonstrated, to increase with age. Although the rate of increase varies considerably in the different classifications, the trend is apparent in each of the sex and race groups. Glover[26] found an increasing incidence with advancing age in a clinical study of hypertrophic arthritis in general. Heine[27] and Keefer et al.[28] have demonstrated it in extensive pathological studies of other human joints. There is experimental evidence of an increased susceptibility to degenerative joint disease with age. Pemberton et al.[29] were able to produce bony spurs on the patellas of old dogs by interference with the blood supply, but were relatively unsuccessful when working with young dogs. Despite these findings, the present study reveals that hypertrophic arthritis of the fingers occurs in the second decade in white men, in the third decade in white women and Negro men and in the fourth decade in Negro women.

Summary

Heberden's nodes (enlargements of the terminal finger joints due to hypertrophic arthritis) occur as a result of direct trauma or arise idiopathically.

A clinical history permits accurate differentiation of these two types, which may otherwise be indistinguishable. An arbitrary classification, based on degree of involvement, has been adopted for this study.

The incidence of both types was determined by examination of nearly 7000 individuals. The incidence was analyzed according to race, sex, age and occupation.

The incidence of both types tends to increase with age in all groups.

The incidence of traumatic nodes is higher in men than in women, is higher in workingmen than in physicians, and is higher in white working people than in Negroes. The differences be-

tween various groups of white people seem to depend on differences in exposure to finger trauma.

The incidence of idiopathic nodes is universally low before the age of sixty, after which it increases very rapidly in white women. It increases much more slowly in workingmen of both races, but remains very low in Negro women.

The low incidence in Negroes of both types of Heberden's nodes is not readily explainable.

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DELINQUENCY*

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CRIME, of all the social problems, is the most interesting. The fact that so many different types of people of all ages are fascinated and intrigued by a criminal career that it is portrayed from many different angles in books, at the theater, on the screen and over the radio, bears witness that crime makes a strong emotional appeal to the masses.

Poverty may be more widely distributed, affect more people, cause more real deprivation, be fundamentally more important as a social problem, but compared with crime it is drab, ordinary, lacking in thrills and held in the contempt which familiarity is said to breed.

Disease, too, as a social problem is without much romance. It may awaken pity or disgust. As a topic of conversation it is often evaded or prohibited as was the public discussion of social diseases until recently. There is a certain morbidity about disease that precludes it from becoming a subject of universal interest. Not so with crime. The more vicious, the more frightful, the more disgusting, the more demoniacally ingenious it may be, the more it is publicized and accepted as a topic for barroom or drawing-room conversation. An atrocious murder by a feeble-minded delinquent would receive more news space than would the discovery of the cause of some baffling disease. Journalists are in the business of giving the public that which it wants and for which it is willing to pay.

There is probably no one answer to the universal interest in crime. One individual is intrigued by the ingenuity with which a particular crime has been carried out. Another is concerned with the sociopolitical aspects of crime in general and the fact that as a business crime has become well established and relatively safe. Some people unquestionably derive a degree of vicarious satisfaction through their interest in the criminal activities of others. In this way they are able to enjoy the freedom from restraint expressed by the antisocial activities of the criminal group, yet remain innocent themselves of open defiance of authority

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and immune to the fear of detection and the feelings of guilt which participation in criminal behavior would invoke. There is no doubt that a large number of highly respected, law-abiding citizens harbor repressed desires to indulge in asocial activity, and find in the criminal activities of others an outlet for these desires. Crime is no longer the activity of the isolated individual. It has become so well organized, so carefully planned, so skillfully executed and so cleverly protected that it must be considered in the light of an epidemic that requires searching investigation in order to determine the source of the contamination, as well as the detection, confinement and treatment of the individuals involved.

There is also a small group of people who go a step farther and attain what appear to be strange thrills through identifying themselves with crime and the criminal activities of others, owing to a strong unconscious urge for adventure or revenge, or perhaps merely the desire to "put themselves across" after repeated failures along socially approved lines. These individuals are the so-called psychopaths. There are many and varied reasons for this morbid psychopathic interest in crime. It is generally recognized that there is no common background for crime, and that we cannot draw any sharp line of demarcation when we consider the varied groups into which criminals fall. Each and every person committing a criminal act must receive individual consideration. However, for purposes of understanding crime as a problem affecting society, we recognize that there are common factors which stand out and appear to give value in an attempt to make some generalizations about the more important biological, sociological and psychological aspects of crime.

The delinquent and the criminal are individuals whose concepts of right and wrong are out of harmony with those of society. There invariably exists a discrepancy between what the delinquent feels he is entitled to in life and what society allows him to have. The aggressive, non-conforming individual, in his effort to evade, avoid or defy the rules and regulations set up by the community in which he lives, eventually finds himself in conflict with the police, probation officer, truant officer and others appointed to maintain so-called law and order.

Delinquent careers do not begin, however, with the child's first contact with the truant officer or the neighborhood policeman, nor do they end after the child has been apprehended and brought before the judge in a juvenile court. Delinquent activity of the chronic type, characteristic of the individuals who fill our correctional institutions, which eventually develops into a life of crime, is not the product of a few days or weeks. The state of mind, the habits, the attitudes and the personality traits that are the basis of criminal careers are in the process of development for years before they receive the official and legal stamp which marks the criminal. In other words, the fundamental basic factors, whether they be biological, sociological or psychological, are usually operating in or on the individual years before his behavior takes on a definite overt criminal pattern.

Every delinquent and criminal must be considered in terms of his own particular and oftentimes peculiar personality make-up, as well as the varied environments and contacts with all their pitfalls and hazards, but for the purpose of acquiring a better orientation to the more important contributory causes of crime, I shall consider for the moment the three main groups in relation to the etiology of crime.

The first is biological and is conditioned by the inherent physical defects or instabilities that are frequently associated with criminal careers and that when operating under certain conditions must be looked upon as being the leading contributory cause.

Mental defectiveness as a cause of delinquency has long been recognized, and its importance as a causative factor has swung through a wide arc. During the early days when psychological tests were being received with unbounded enthusiasm, mental deficiency was given the most important place in the etiology of crime. For example, Sutherland,[1] on reviewing the statistics on this subject, found that from 1910 to 1914 there were 50 per cent feeble-minded patients among delinquents; from 1915 to 1919, 28 per cent; from 1919 to 1924, 21 per cent; and from 1924 to 1928, 20 per cent. The last figure is a fairly conservative estimate of the frequency of mental deficiency among delinquents, but it is necessary to point out that as a cause of crime it must not be considered alone but must be studied in relation to other factors.

The relation between mental retardation and juvenile delinquency should not be difficult to determine. However, in the literature there does not appear to be any consensus on the subject. Thompson,[2] of the Department of Hospitals, Psychiatric Clinic, Court of the General Sessions, New York City, states: "The percentage of defectives is no greater among criminals than among the civil population. Therefore, mental defect cannot be given a prominent place as a factor causative of crime." On the other hand, Glueck,[3] in her investigations relating to mental retardation and juvenile delinquency, states:

> (1) There is a far higher proportion of children of lower intelligence among delinquent groups than

in the general population of children; (2) the likelihood of delinquency among children of lower intelligence is greater than among those of higher intelligence; and (3) the families of young delinquents of lower intelligence are far less able than those of higher intelligence to participate constructively in any program for the supervision and treatment of such children.

My own experience would lead me to agree with Glueck's conclusions. In a recent study of a group of predelinquent children which were followed up over a period of ten years or more, I was impressed with the fact that there was a far greater tendency for the predelinquent children under ten years with low I.Q.'s to continue a life of delinquency than there was for the children with high I.Q.'s. This does not necessarily mean that a poor intellectual endowment of itself is the cause of delinquency. It does mean, however, that under the existing social and economic conditions these children are subjected to stresses and strains of life of such a nature and of such intensity that failure to meet them successfully is almost inevitable, unless they are given special aid in making a place in the social and economic world.

Mental disease, although rarely diagnosed in children during the first decade, is undoubtedly in the process of development, and some of the strange, peculiar, unpredictable behavior during this early period, as well as the less obvious evidences of personality disorder, are but the beginnings of mental abnormalities. The inherently shy, diffident, shut-in type retreats from the scene of conflict and evades competition by protecting himself with a neurosis, while the more aggressive often finds delinquency an avenue of escape.

In passing, one can only mention the asocial activity associated with epilepsy, encephalitis lethargica and the abnormal behavior which frequently follows damage to the nervous system occurring at all ages.

Considerable attention has been given to the role which the endocrine glands play in affecting behavior. Lurie[4] found that 20 per cent of the behavior disorders studied at the Child Guidance Home in Cincinnati, Ohio, showed endocrine disturbances, and that in 93 of the 1000 cases studied there was a direct relation between the glandular dysfunction and the behavior difficulty. Rowe,[5] in his analysis of 104 cases of behavior disorder in children, found that 68 had an associated endocrine disorder. Whether or not these figures exaggerate the extent to which glandular dysfunction is associated with behavior is not so significant as the fact that careful investigation of the physical side of the child's life is of importance.

The psychiatrist as a specialist in the field of mental aberrations, and as a physician, has a valuable contribution to offer in this particular field. Therapy so far as these biological defects and acquired handicaps are concerned depends very largely on the early recognition of the problem in order that adequate study, treatment, care and supervision can be instituted. Recidivism should be materially curtailed by the early recognition of the group of delinquents who are not likely to profit from experience. Victims of crime, grief-stricken parents and irresponsible delinquents would all profit by an early recognition and an intelligent plan of supervision. The defectives as a group are problems only when poorly adjusted.* When they are recognized early, a plan for training can be instituted which will permit many of them to fit into a social scheme of life on a certain level so that they may evade competition with those intellectually superior, and avoid inevitable failure, which so frequently leads to delinquency. One must keep in mind that crime is not being considered as a biological problem per se, but that the fact is being recognized that there exist biological handicaps which are conducive to criminalistic behavior.

The largest and by far the most important group in our etiologic classification are those delinquents whose asocial behavior can be attributed to a very large extent to sociological factors which need not be considered permanent, inevitable or irresistible to change. In fact, demonstrations[6] have already been made showing conclusively that the delinquent rate in certain city areas is many times higher than it is in others, that in some of these areas as many as 15 to 25 per cent of the boys between the ages of ten and seventeen are arrested for delinquency in any one year, and that approximately 43 per cent more of the delinquents in the delinquency areas are recidivists than in the outlying neighborhoods where the rates are relatively low. Furthermore, delinquency rates can be reduced by improving the sociological conditions under which these individuals have to live.

I need not enter into any prolonged discussion at this time as to the relative importance of environment and heredity, since I am not embarking on a dissertation to prove that environment and its sociological pitfalls are the cause of all delinquency. I am simply stating that as one of the leading factors contributing to delinquency, they warrant serious attention. It is an undisputed fact, and has been shown over and over again, that delinquency is frequently associated with poverty, vice and disease.

*Dr. Walter Fernald, a keen student in the field of mental deficiency, entertained the idea for years that mental deficiency was relatively rare, that defectives were all potential delinquents and that they should all be in institutions. With the courage characteristic of a great man, in the latter part of his life he reversed these opinions and conceded that, while there were many defectives, few were bad and only a small portion should be in institutions.

A brief review and comparison (Table 1) of the results found in two investigations — the first by the Gluecks,[7] in which the social background

TABLE 1. *Effect of Social Background.*

SOCIAL BACKGROUND	WELL-ADJUSTED GROUP	DELINQUENT GROUP
	%	%
Home and neighborhood:		
Home conditions average or better	78	38
Neighborhood conditions average or better	95	15
Economic status:		
Families dependent or on verge of dependency	13	76
Employment of mothers:		
Mothers gainfully employed	14	42
Nativity of parents:		
Native-born parents	Over 60	20
Education of parents:		
Illiteracy	Less than 1	29
Attended or graduated from high school	46	10
Attended or graduated from college	Over 29	1
Age of parents at marriage:	yr.	yr.
Mean age of parents	25.5	
Mean age of younger parent		21.5
Difference in parents' ages:		
Mean difference in age between parents	3	Almost 6
Marital adjustment:	%	%
Parents living together congenially	90	62
Contacts with social agencies:		
No contacts with agencies	78	13
Broken homes:		
By death of one parent	18	
By divorce	2	
By death of one or both parents		27
By desertion, separation or divorce		19
By criminality of one or both parents		20
Size of families:		
Large family (5 or more children)	11	58
Mean number of children per family	2.93	4.98

of a group of juvenile delinquents was presented, and the second by Thom and Johnston,[8] in which the social background of a group of well-adjusted adolescents was studied — indicate at least the importance of environment and the contribution that it makes to the development of habits, attitudes and personality traits, and other indefinable mental and emotional characteristics that tend to produce stable, conforming, happy, efficient and mature adults, on the one hand, or asocial, non-conforming, law-evading delinquents, on the other.

Striking as these statistics are, one should not jump to the conclusion that bad neighborhoods, poverty, broken homes, alcoholic fathers and psychopathic mothers are necessarily the cause of criminal careers in all the Gluecks' cases, or that the preponderance of good homes, sober, industrious parents and happy marital situations necessarily produces well-adjusted children. There would be too many exceptions to such a rule to allow any but the most gullible to be satisfied with such an answer. Nevertheless, it cannot be ignored that when certain types of children are subjected to these contaminated social situations, it is just as natural and normal for them to turn toward delinquent careers as it is for them to learn to speak English when brought up in an English-speaking home.

I was much impressed by the statement by Partridge,[9] of the Boy Scouts of America, which reads as follows:

> In the great majority of cases young people are measured against an adult scale which is quite foreign to them and not in keeping with the set of values they are maintaining with their immediate associates. The fact that they are more disposed to follow the edicts of their fellows than respond to the intangible will of the law, is not difficult to understand because of the definition they have accepted of themselves. It is very important that the individual maintain this with his own immediate group. A happy adjustment to their associates is of relatively greater importance than the possibility that they will be punished by adult society. As a matter of fact, it is not uncommon for groups of young people to consider it an honor among themselves to come into open conflict with the law. The nature of the law is painted to them as a force which is against their own interests; it chases them off the streets; it makes them go to school; it punishes them when they are caught. Keeping in good with their gang and still not getting caught comes to be a game, and those who are the most successful in playing it become the heroes of the group.
>
> And thus it is that young people come into delinquent acts in the most moral and natural way that can be imagined. It is not as if they deliberately planned to run adverse to society. Young people usually get into trouble in the pursuit of natural impulses arising from their own biological needs. In following the traditions of their own group, young people carry on until certain numbers of them are caught up in difficulties. The great majority outgrow these tendencies; those who do not become our chronic delinquents. Many would outgrow their difficulties if given half a chance. Some are definitely started on a career of crime by the way in which they are treated when they get into minor trouble.

Psychiatry as a branch of medicine is concerned with mental aberrations, whether they be emotional or intellectual, not only those which prevent the individual from making the necessary adjustments to life so that he can conform in a satisfactory way to his environment and live in harmony with the group, but also those emotional states which create internal conflict and interfere with the individual's happiness and efficiency.

Mental hygiene is the preventive aspect of psychiatry, and is concerned with the development and preservation of mental health. Mental health is a state of mind which permits the individual to approach his maximum efficiency and to attain the greatest amount of happiness out of life with a minimum amount of friction, anxiety and guilt.

The administration of the principles underlying mental hygiene need not necessarily be confined to the realm of the psychiatrist, any more than physical hygiene needs to be administered exclusively by a physician. In fact, I believe that until men-

tal hygiene can be reduced to such terms that it can be utilized in the everyday practice of the parent, teacher, nurse, physician, probation officer and others concerned with the training and education of children, it will not serve a very useful purpose or affect advantageously an appreciable portion of the general public. Such a concept of mental hygiene in no way relegates the psychiatrist to obscurity. There are a sufficient number of intricate, involved, complex problems in the field of delinquency that cannot be interpreted in terms of the individual's environment where the case-work method of the sociological school fails to fathom the depth of the inner strivings, frustrations and phantasies, and the morbid, distorted, twisted operations of a sick mind.

If delinquency is to be prevented, the attack must be made at its source, during the predelinquent stage, when character is in the process of development. During childhood the habits, attitudes, personality traits, opinions, beliefs, concepts of right and wrong, sense of responsibility and feeling of obligation to those other than self are being incorporated in the fabric of the individual's personality. The first decade, particularly the preschool years, is by far the most important in this respect. There can be no substitute for home training, not even in the school or church, much less the psychiatric clinics and juvenile courts. Probation and all the other valuable and influential agencies which have resulted in our new philosophy toward delinquency are but aids after the individual has failed to attain his place and adapt himself to the demands of his environment.

There is no doubt that in an effort to prevent or perhaps minimize the effect of these adverse sociological factors, mental hygiene and the application of psychiatric principles have a contribution to make. Frequently the underlying motivating forces, such as inferiority feelings, resentment toward authority, rebellion against dependence and such unhealthy emotions as jealousy, cruelty, pugnacity, revenge, which are subsequently manifested toward society, were originally unconsciously cultivated toward and because of individual circumstances and conditions operating during the early years. The psychiatrist working directly with the individual may so reorient his point of view, as well as that of the adults who play a vital role in his experience, that the sociological readjustments brought about by the case worker will be acceptable. This psychological approach of preparing the child for accepting new habits and attitudes toward the improved social conditions under which he may be permitted to live need not necessarily be turned over to a psychiatrist or a clinic. As stated before, these principles must be reduced to such terms as can be practiced by all those who are exerting an influence in the development of the child.

To psychiatry and other allied groups belong those cases of delinquency resulting from biological defects and acquired handicaps of a physical or mental nature, where wise and practical therapy for the delinquent and protection to society depend almost entirely on making the correct diagnosis. Therapy as indicated in these cases must be carried out in co-operation with parents, teachers, social workers, juvenile court judges and probation officers, and not infrequently under the medical direction and occupational supervision that can be rendered only in a well-organized institution.

More strictly confined to the field of psychiatry are those delinquents whose asocial activities result from mental aberrations due to psychological causes. Delinquent or nonconforming behavior is not so different from conforming behavior psychologically as it is socially. All behavior represents an effort on the part of the individual to find satisfactory outlets for a varied sort of ill-defined emotional drives — desires, appetites, urges, call them what you will. When inherent limitations, social conditions, economic deprivations and excesses of mental stress and physical strain have imposed restrictions and subjected the individual to failure that is as inevitable as it is continuous, the usual socially approved adaptations to life break down, and conflicts, frustrations, repressions, fears, obsessions and resentments begin to dominate the individual, affect his behavior and create an unhealthy, distorted outlook on life. When these psychologically and sociologically induced forces create a situation which the individual can no longer cope with in a normal, rational way, something happens. It may be a convulsive explosion, a hysterical paralysis, or a more elaborately developed neurosis with many incapacitating and protective symptoms (all physical expressions of mental conflict), or perhaps these conflicts may express themselves in abnormal conduct of which delinquency may be a manifestation.

It is especially in the study and investigation of these peculiar, apparently unreasonable expressions of mental conflict that psychiatry has a contribution to make. Psychiatry is not a panacea in the treatment of delinquency. There is ample evidence of the limitations which our lack of knowledge regarding human nature has imposed. Psychiatry has, however, during the last two decades evolved an approach to the study of delinquency comparable to that utilized in the field of general medicine. Psychiatry is primarily concerned with

the delinquent rather than with his delinquency. It shares with medicine the scientific point of view that leads to the search for the cause rather than being preoccupied with the symptoms.

The early stages in the development of a delinquent career are as well marked as they are in the development of a disease process. It is regrettable, however, that we have not a few of the instruments of fine precision to measure and evaluate our findings in dealing with human conduct as we have in physical research. There is no sharp line separating the psychological from the sociological approach in the study of delinquency and its prevention.

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REPORT ON MEDICAL PROGRESS

THE VITAMINS*

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IN TWO previous reviews[1, 2] appearing in this series, an attempt was made to give a brief summary of present-day knowledge regarding the vitamins. This field is developing with such rapidity at the present time that what was written a year ago is already behind the times in several respects. The following supplementary review has therefore been prepared to bring the previous summary up to date.

VITAMIN A

Interest in vitamin A deficiency continues to center in the important subject of nutritional night blindness. The problem of measuring correctly the degree of subnormal adaptation to darkness is still the subject of extensive research. So far there is no general agreement as to the best procedure and the type of instrument most suitable for this purpose. Critical reviews of the difficulties involved will be found elsewhere.[3, 4] Until the method is standardized and the correct interpretation of the readings is more clearly defined, it would seem inadvisable to adopt such procedures as an aid to the routine diagnosis of nutritional deficiency. For the same reason it is probably wise at present to withhold judgment on the significance of reports based on such procedures concerning the incidence of nutritional night blindness in the community.

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THE VITAMIN B COMPLEX

Riboflavin Deficiency

In last year's review[2] on the water-soluble vitamins, reference was made to the fact that although at that time riboflavin deficiency had not been recognized in man, nevertheless riboflavin was probably important in human nutrition, because it had been shown to be the active component ("prosthetic group") of Warburg's "yellow enzyme," which apparently plays an extremely important role in the oxidative mechanisms of the tissues. Since the publication of that review clinical evidence of riboflavin deficiency has been obtained.[5] Eighteen women were fed for a long period on a deficient diet essentially similar to that which is taken by the inhabitants of districts where pellagra is endemic. Thirteen of these women developed characteristic lesions of the mouth and face. The lesions did not respond to nicotinic acid therapy, but were cured by the administration of pure synthetic riboflavin. The nature of these lesions is threefold. There is maceration and fissuring at the angles of the mouth, a type of lesion formerly referred to as perlèche or angular stomatitis. The mucous membrane at the line of closure of the lips is red and denuded; the name "cheilosis" has been proposed for this lesion. Finally, there is a scaly, greasy desquamation in the nasolabial folds, on the alae nasi, in the vestibule of the nose and sometimes on the ears and eyelids. Angular stomatitis had been previously recognized in many parts of the world as a man-

ifestation of deficiency disease. It is commonly present in pellagra and in Oriental beriberi,[6] and has also been described as occurring in the absence of other evidence of vitamin B complex deficiency. That it occurs in association with deficiency of the vitamin B_2 or heat-stabile fraction of the complex had been recognized previously.[7,8] Further work will have to determine whether these lesions can always be accepted as evidence of riboflavin deficiency. It may turn out eventually that they are merely a nonspecific manifestation of poor nutrition, though readily curable by one particular nutritional factor when lack of this factor is the principal deficiency present.

Though riboflavin has been isolated and synthesized as a yellow crystalline powder, with the formula $C_{17}H_{20}N_4O_6$, it is still an expensive product. For this reason, and also because of their possible non-specificity, perlèche and cheilosis should be treated not with pure riboflavin but with yeast or crude liver extract, which are good sources of riboflavin, and at the same time contain other nutritional factors which may be of value in the particular case concerned.

Vitamin B (Complex) Deficiency

In recent years it has come to be realized with increasing clarity that the syndromes known as beriberi and pellagra are not the result of deficiency of a single dietary factor, but are the clinical consequence of multiple deficiencies involving several components of the vitamin B complex, and sometimes other dietary factors in addition. Moreover, although the classic syndromes of pellagra and beriberi are rarely encountered except in those parts of the world where they are endemic, some of the features of both these syndromes occur, with much more frequency than was formerly realized, in cases seen in other communities.

Deficiency of the vitamin B complex is liable to arise not only from faulty diet but also from defective absorption and from an increase in the nutritional needs of the body. This deficiency therefore is sometimes encountered in patients who can afford an ample and varied diet. In alcohol addicts, for instance, a polyneuritis of nutritional origin may occur, which though often mainly the result of poor eating habits is partly due to the fact that certain components of the vitamin B complex are utilized with unusual rapidity when the caloric consumption (in the form of alcohol) is abnormally high. A similar polyneuritis may occur in pregnancy, often partly as a result of loss of food by repeated vomiting, but also because of the increased nutritional requirements of pregnancy. Defective intestinal absorption is probably the principal factor in the production of polyneuritis occurring in patients suffering from organic lesions of the gastrointestinal tract. In these various conditions the type of polyneuritis is in every way similar to the polyneuritis of beriberi, and almost certainly has the same fundamental etiology.

The principal clinical manifestations of vitamin B deficiency are enumerated below.

Pellagrous dermatitis. This is mainly due to nicotinic acid deficiency, but, as it occurs on the face, may partly result from riboflavin deficiency (see above). Occasionally another type of dermatitis, due to vitamin A deficiency,[6,9] may occur in association with vitamin B deficiency, particularly in beriberi.[6] This is manifested by the presence of hyperkeratotic plugs in the sweat glands, dry skin and absence of sweating. It has been recently claimed[10] that hyperkeratosis of the skin follicles around the nose is due to riboflavin deficiency, but this seems doubtful.

Angular stomatitis. This is frequent in many deficiency states. Its relation to riboflavin deficiency has already been discussed.

Glossitis. In endemic pellagra, this is the result of nicotinic acid deficiency, but it is due to other causes in some other nutritional disorders.

Diarrhea and perianal inflammation. This occurs in pellagra, owing to nicotinic acid deficiency.

Polyneuritis. This is frequent in beriberi, pellagra and other nutritional disorders; it is commonly thought to be due to thiamin (vitamin B_1) deficiency.

Degenerative changes in the spinal cord. These occur in severe pellagra and beriberi; they are perhaps due to deficiency of the undefined factor, whose deficiency is also responsible for combined system disease associated with pernicious anemia.

Psychosis. This is frequent in pellagra and occasionally occurs in beriberi.[6] Acute psychosis associated with vitamin B deficiency usually responds dramatically to nicotinic acid therapy. Longstanding pellagrous dementia responds less well, and Korsakoff's psychosis probably not at all, indicating the operation of some other factor or the development of irreversible structural changes.

Cardiovascular changes. These include tachycardia, cardiac dilatation, peripheral vasodilatation, edema and tendency to fatal syncope; they are common in beriberi and are probably a direct result of thiamin deficiency, although coexisting protein deficiency and consequent hypoproteinemia may sometimes play a part in the production of edema.

Anemia. This is sometimes severe in deficiency disease in the tropics, and is common in deficiency

associated with alcoholism; it is due to deficiency of some as yet unidentified nutritional factor, possibly identical with the dietary factor, which if not acted on by the intrinsic factor of the stomach leads to pernicious anemia. Anemia occurring in cases of vitamin B deficiency may be due also to other causes.

Porphyrinuria. It has been repeatedly stated recently that porphyrinuria is a characteristic feature of pellagra. However, it has been shown[11, 12] that the test for porphyrin employed in the work on which these statements are based is not a test for porphyrin. It has not yet been proved that porphyrinuria can be caused by pellagra. It does occur in cases of pellagra associated with alcoholism and liver disease, and in such cases is quite probably due to the liver disorder.

Each of the foregoing manifestations is liable to occur in association with one or more of the others in any particular case of vitamin B deficiency, depending on which factors in the complex are chiefly lacking from the diet. The fact that endemic pellagra and beriberi usually present a clear-cut clinical syndrome is probably due to the uniformity of the diet in the locations where they occur. Elsewhere the clinical picture is far more diverse, coincident with a greater variety in the composition of inadequate diets. The multiple causation of the clinical features in most cases of vitamin B deficiency renders it particularly important to treat such cases with some preparation which will supply all the various elements in the complex. Yeast concentrates and crude liver extract are particularly suitable for this purpose. A complete, high-caloric diet is also necessary to supply other important dietary essentials which, though usually not sufficiently lacking to produce any definite manifestations, are very frequently taken in insufficient amounts by subjects showing evidence of vitamin B deficiency. The pure synthetic vitamins now available should be considered only as a useful addition to this treatment, for employment in cases where evidence of deficiency of one particular factor is outstanding.

Therapeutic Use of Nicotinic Acid

The conclusions reached last year[2] concerning the use of nicotinic acid in the treatment of the outstanding features of pellagra have been confirmed in most respects by subsequent work. The original optimistic report[13] of its use in the cure of the psychotic symptoms has been somewhat revised. It is now admitted[14] that some cases with long-standing mental symptoms respond only partially to nicotinic acid therapy. As pointed out above, some part of the dermatitis in pellagra may be due to riboflavin and vitamin A deficiency, and therefore will not be affected by nicotinic acid therapy. A report[15] based on a careful study of the use of nicotinic acid in the treatment of pellagra indicates that 200 to 300 mg. per day taken by mouth is a suitable therapeutic dose. The opinion of one experienced observer[16] concerning the use of nicotinic acid is "enthusiastic, but not quite as enthusiastic as are many others about the value of the drug."

The Therapeutic Use of Thiamin

Despite the numerous statements in the recent literature that nutritional polyneuritis is due to deficiency of thiamin, I still believe that the evidence on which these statements are founded is not sufficient to justify the treatment of an uncomplicated case of nutritional polyneuritis with thiamin only. Although additional thiamin may be beneficial, adequate treatment should include an ample and nutritious diet, together with some preparation of yeast or crude liver extract.

Ascorbic Acid (Vitamin C)

There is little new knowledge concerning vitamin C. The successful use of an injectable form of the vitamin has been reported.[17] An excellent review of present-day knowledge regarding the diagnosis of vitamin C deficiency and the therapeutic use of ascorbic acid will be found elsewhere.[18]

Vitamin D

Dihydrotachysterol (A.T. 10) has been successfully used in the treatment of hypoparathyroidism. This substance is very closely related chemically to vitamin D and has some of the same biological properties. It facilitates the absorption of calcium from the intestines, but has a more marked effect than does vitamin D in increasing the urinary excretion of phosphorus, which is probably the reason why it is not effective in rickets.[19] These properties make it peculiarly suitable for the treatment of hypoparathyroidism. It has been pointed out[20] that a patient with hypoparathyroidism may take A.T. 10 in much the same way as insulin is taken by patients with diabetes, the dose being controlled by a simple test for calcium in the urine.

Vitamin K

Knowledge concerning vitamin K has advanced with extraordinary rapidity during the last year. This knowledge is certainly the most outstanding achievement of nutritional science since the discovery of the pellagra-preventing activity of nic-

otinic acid two years ago. No attempt can be made here to review all the recent literature on vitamin K. The following account is confined to a brief summary of the present status of this vitamin. For a more complete account the reader is referred to two very helpful reviews[21, 22] which have appeared during the last year.

Chemistry

Following the successful isolation of vitamin K by several independent groups of workers,[23–25] recognition of its chemical composition soon followed. It was found to be related chemically to the substance phthiocol, which had been previously isolated from tubercle bacilli[26] and has now been shown to possess vitamin K activity.[27] As in the case of vitamin D, it is realized that vitamin K is not a single chemical entity, and that several closely related compounds possess vitamin K activity. They are all related chemically to naphthoquinone. Natural vitamin K_1 obtained from alfalfa has a slightly different chemical composition than has vitamin K_2 isolated from putrefied fish meal.[28] Vitamin K_1 has now been synthesized.[29, 30] At the present time it appears[31] that 2-methyl-1, 4-naphthoquinone is the most active of the synthetic compounds so far studied. The relative simplicity of these active synthetic compounds should enable them to be manufactured on a considerable scale, and before long they will doubtless be freely available for general use.

Physiology

Vitamin K was first recognized in 1935 from the fact that chickens fed on a diet deficient in this vitamin developed hemorrhages. The bleeding was apparently due to a fall in the concentration of prothrombin in the blood. According to the Howell theory of blood coagulation, prothrombin is the substance which in the presence of calcium and thromboplastin yields the active substance thrombin. Thrombin then converts fibrinogen to fibrin, thus bringing about coagulation. It is now believed that vitamin K is essential for the normal synthesis of prothrombin in the body, and perhaps is actually the active component (or "prosthetic group") of this substance. Apparently the liver plays a very important part in this synthesis.[32] Vitamin K, like other fat-soluble substances, requires the presence of bile salts to facilitate its absorption from the intestinal tract.[33] It is probably present in many common foodstuffs. The vitamin is produced by other bacteria besides the tubercle bacillus, including those present in the intestines, and these may provide an important source of the vitamin.

Human Pathology

Vitamin K deficiency and consequent hypoprothrombinemia may result from inadequate intake or from defective intestinal absorption. In addition, hypoprothrombinemia may occur as a result of failure of the liver to utilize vitamin K in the synthesis of prothrombin.

Inadequate intake. It has been shown[34] very recently that adult individuals partaking of an inadequate diet may show a reduced concentration of prothrombin in the blood, and that the administration of vitamin K will correct this abnormality. It has also been shown that in newborn infants,[35, 36] and perhaps particularly in premature infants,[37] there may be a similar reduction in the level of prothrombin in the blood which usually responds to the administration of vitamin K. It has been suggested that this deficiency is due at least in part to delay in establishing in the bowel the normal bacterial flora which is able to synthesize the vitamin.[38] This discovery is obviously of the greatest importance in relation to hemorrhagic phenomena in the newborn, and it seems likely that administration of vitamin K to the mother prior to delivery might materially lessen the incidence of intracranial bleeding and other types of hemorrhage in the newborn.[37]

Defective absorption. In the absence of an adequate secretion of bile, vitamin K absorption is impaired and hypoprothrombinemia is liable to result. It now appears[39] that this is the explanation of the bleeding that occurs in cases of obstructive jaundice, and that has been responsible in the past for nearly a fifth of the operative deaths in the surgical treatment of patients with jaundice. It has been clearly demonstrated by several groups of workers[40–42] that in most cases of obstructive jaundice with bleeding tendency, the oral administration of vitamin K together with bile salts is effective in increasing the prothrombin level in the blood and in checking the hemorrhage. Vitamin K deficiency conditioned by defective intestinal absorption may also occur as a result of intestinal obstruction, surgical short circuits and certain disorders associated with diarrhea, such as ulcerative colitis and sprue.[43]

Defective prothrombin synthesis. It appears that in certain primary diseases of the liver the synthesis of prothrombin may be impaired, despite an adequate intake of vitamin K. In these conditions administration of vitamin K is less likely to be successful in raising the prothrombin level of the blood and preventing hemorrhage.[40]

Diagnosis

At the present time there is no method of meas-

uring directly the amount of prothrombin in the blood, but an indication of this amount can be obtained by measuring in the test tube the time taken for the blood or plasma to clot, after precautions have been taken to see that all other substances necessary for clotting are present in excess, and that the amount of prothrombin is therefore the only limiting factor. In practice the method of Quick[44] appears to be the most convenient and reliable for ordinary clinical purposes. The only practical difficulty in the use of such tests as a routine laboratory procedure is that of obtaining a satisfactory source of thromboplastin to ensure an adequate concentration of this substance in the material to be tested. It is probable, however, that before long some stable preparation of thromboplastin will be found. The method will then become a simple matter that can be carried out in any routine laboratory. One difficulty in interpreting the significance of prothrombin times is that the time does not become significantly prolonged until the level of prothrombin in the blood has fallen considerably, perhaps almost reaching the point at which hemorrhagic phenomena are liable to appear. For this reason the demonstration of a normal prothrombin time in a case of jaundice prior to surgical operation is no guarantee against a dangerously low level of prothrombin in the blood, and is certainly no insurance against postoperative hemorrhage. Lesser degrees of hypoprothrombinemia can be demonstrated if necessary by diluting the plasma with additional plasma rendered free from prothrombin[34]; the consequent reduction in prothrombin concentration may demonstrate a deficiency of prothrombin in specimens which, undiluted, show a normal prothrombin time.

Treatment

At the present time the indications for the administration of vitamin K as a prophylactic measure appear to be as follows: It should be given to expectant mothers shortly before delivery. Its use is indicated in cases of intestinal obstruction, surgical short circuits of the intestines and conditions associated with chronic diarrhea. It is worthy of trial in chronic liver disease, but is peculiarly valuable in the preoperative and postoperative treatment of cases with obstruction of the common bile duct.

Vitamin K is of the greatest value in the treatment of hemorrhagic disease of the newborn, and in bleeding associated with obstructive jaundice. It will probably be found effective in cases of bleeding associated with disorders of the alimentary tract when ascorbic acid deficiency is not the cause. It should be tried in bleeding associated with primary diseases of the liver. It is almost certainly not effective in hemorrhagic conditions such as hemophilia and purpura hemorrhagica.

Methods of Administration and Dosage

Oral administration is usually effective. In cases where the secretion of bile is impaired, bile salts in capsules (2 to 4 gm.) should be given together with the vitamin. When the bleeding is severe and the condition urgent, administration by duodenal tube has been recommended.[40] Some preparations of vitamin K can also be given parenterally; the efficacy of this route of administration is at present undergoing trial.

No recommendation as to dosage will be made in this review, since the advent of synthetic vitamin K has rendered obsolete all previous reference to doses in terms of arbitrary standard units. Units defined in terms of pure synthetic vitamin will probably be adopted very shortly, and until that time the reader will find adequate recommendations elsewhere[22] as to appropriate doses in terms of the units at present employed.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTEMORTEM AND POSTMORTEM RECORDS AS USED IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 26081

PRESENTATION OF CASE

A fifty-five-year-old Italian woman was admitted to the hospital complaining of pain in the right flank.

Two years before admission the patient developed polydipsia and polyuria, and a diagnosis of diabetes mellitus was made in an outside dispensary. Since that time a daughter had tested her mother's urine at least twice a week and had given her insulin according to the test. Further information regarding the diabetes was not obtainable.

The patient was allegedly well until seven days before entry when she noticed a "tickling" sensation about the urethral meatus during urination, associated with frequency and nocturia. Four days before admission she developed a constant steady pain, located in the right flank and right costovertebral area, which occasionally radiated downward into the right groin; this aching discomfort persisted until admission. She also developed a slight nonproductive hacking cough, which at times made her flank pain more severe. No chills, fever or other genitourinary, cardiorespiratory or neuromuscular symptoms were noted. The patient had been pregnant twenty-seven times. Eight children had died in infancy, and there had been ten miscarriages. The menopause had occurred four years before admission. The remaining family, marital and past histories were negative.

The physical examination revealed a corpulent, flushed woman who lay flat in bed, moaning and groaning. Her respirations were rapid and shallow. Examination of the heart, lungs, abdomen and extremities was negative. There was an erythematous moist rash about the pubic region. The pelvic and rectal examinations were negative. The blood pressure was 110 systolic, 70 diastolic.

The temperature was 102.4°F., the pulse 90, and the respirations 32.

Examination of the blood showed a red-cell count of 5,050,000 with 85 per cent hemoglobin, a white-cell count of 15,400 with 84 per cent polymorphonuclears, and a normal smear. The urine was slightly turbid and had a pH of 5, a specific gravity of 1.020 and a ++ albumin test; in the sugar test it was green with a yellow sediment; acetone and diacetic acid were absent. The sediment was negative for red cells, but contained innumerable clumps of white blood cells and a few coarse granular casts. Abundant colon bacilli were cultured from the specimen. The stools were brown, soft, formed and guaiac negative. The blood Hinton test was negative. The admission blood sugar was 640 mg. per 100 cc., the carbon-dioxide combining power 24 cc. N/10 carbonic acid, and the nonprotein nitrogen 63 mg. A blood culture showed no growth. Serum Widal and undulant fever agglutination tests were negative.

Roentgenograms of the lumbar spine and pelvis showed lipping along the articular margins consistent with a moderate degree of hypertrophic arthritis. The large bowel contained a moderate amount of gas and fecal material. No grossly dilated intestinal loops were visible. Films of the chest showed that the diaphragms and lower lung fields were obscured by large breasts. The lung fields were clear so far as they were shown on the films. Maximum x-ray exposure did not succeed in outlining the bases. The heart was within the upper limits of normal. Retrograde pyelograms showed a normal kidney pelvis and ureter on the left side. The greater portion of the right kidney pelvis was filled and appeared normal.

The patient remained in the hospital twenty-nine days, during which time, for the first two weeks, she ran a constantly elevated but spiking fever, ranging daily from 101 to 102.6°F. The pulse varied similarly from 90 to 120, and the respirations were elevated between 30 and 45. For the last two weeks the temperature spiked more widely, and gradually rose to 105°F. before her demise; the pulse and respirations rose to 140 and 50 respectively.

She was placed on a diabetic dietary regime and was given insulin, and in three days after admission the blood sugar was 272 mg. per 100 cc. It was maintained around this figure for the remainder of her illness; on one occasion, two weeks after entry, it was 155 mg. She was maintained thus on approximately 30 units of insulin a day. The urine sugar tests were green with sediment or blue, and the diacetic and acetone tests were all negative.

Because of the patient's urinary infection, sulfanilamide was administered to a blood level of 6.6 mg. per 100 cc. on the eighth hospital day. The red-cell count on the tenth day was 3,170,000 with 62 per cent hemoglobin, and the white-cell count 18,000. The patient failed to respond, the urine continued to show abundant colon bacilli, and the pyrexia persisted. On the eleventh day the sulfanilamide blood level was 9.5 mg. per 100 cc. On the thirteenth hospital day the red-cell count had

fallen to 2,700,000, and the leukocytes were 11,400. Sulfapyridine was substituted for sulfanilamide for the next four days. On the fourteenth day the patient received a 500-cc. transfusion, and during the next fourteen days three similar transfusions were administered. From the eighteenth to the twenty-seventh hospital day sulfanilamide was again given to the patient, 1.0 gm. four times a day. The red-cell and white-cell counts fell slowly and steadily, in spite of transfusions, to 2,490,000 and 7300 respectively on the twenty-fourth hospital day. On the twenty-fifth day a van den Bergh was 2.0 mg. per 100 cc., biphasic; a bromsulfalein test gave 50 per cent retention of the dye; the carbon-dioxide combining power and serum chlorides were within normal limits. On the twenty-eighth day the red cells were 1,640,000, the white cells 400. The smear showed a few lymphocytes but no granulocytes. The patient became delirious, developed Cheyne-Stokes respirations, failed and died on the next day.

Differential Diagnosis

Dr. Charles L. Short: May I see the x-ray films?

Dr. George W. Holmes: I do not believe I can add anything to the description given in the text. Certainly the diaphragm is high. She was a large heavy woman, apparently, and the poor aeration could be explained the way it was in the report. There is nothing characteristic about the chest films. Those of the pelvis, taken after the retrograde injection was made, are not complete, but I do not see anything characteristic about them. I should think they would be interpreted as negative.

Dr. Short: I think we can accept the diagnosis of diabetes in this patient without question. She was undoubtedly a mild case in a middle-aged individual who had a high threshhold for sugar, perhaps due in part to renal infection with diminished renal function. Further evidence that it was a mild case is the fact that she developed no acidosis in spite of the infection. During the course of the patient's illness the diabetes was well controlled, and I do not believe we can say that it bore any direct relation to her death.

We can also accept the diagnosis of urinary infection due to the colon bacillus, presumably with pyelitis and pyelonephritis. There is no evidence from the pyelograms or clinically of any urinary obstruction, but with twenty-seven pregnancies she may well have had a cystocele that contributed.

The patient was treated with sulfanilamide. That was started on the eighth hospital day and on the tenth the red-cell count was 2,000,000 lower than on admission. It would be interesting to know what the count was the day before sulfanilamide was started — in other words, whether this was a fall over two days or whether the count had been falling steadily because of her infection. Three days later there was noted a further fall in the red-cell count to below 3,000,000. At this point sulfapyridine was substituted for three days, either because of the anemia the patient was developing or possibly because the infection was not being controlled by the sulfanilamide. From then on the patient was given sulfanilamide until two days before her death. She had four transfusions, but the red-cell count remained level for a while and finally fell off still more. Then she developed jaundice, with a positive van den Bergh test, and died with a red-cell count of 1,600,000 and an agranulocytosis.

The question that must be decided at the outset is whether the anemia or agranulocytosis could have been due to anything besides drug toxicity. I think we must assume that the blood changes were due to the sulfanilamide and sulfapyridine rather than to the infection, but of course in any patient with severe infection and receiving sulfanilamide that point cannot be definitely settled ante mortem. The jaundice I should rather ascribe to the hemolytic type of anemia that characteristically occurs after sulfanilamide than to any form of liver damage secondary to the infection. A depressed liver function is observed in cases of severe hemolytic anemia associated with sulfanilamide, probably due to anoxia of the liver cells. The diphasic van den Bergh is also compatible with a hemolytic anemia and does not predicate primary liver damage. It would be helpful to know what the blood smears showed during the course of the disease — as to whether there was any reticulocytosis or other evidence of regeneration, also, whether there was urobilinogen in the urine.

The continued fever toward the end may well have been due to drug toxicity rather than to the original infection, but there is no way of proving that, and it is often a difficult decision to make in a patient who is receiving sulfanilamide. An aplastic form of anemia does rarely occur with sulfanilamide and that is a possibility here, since we do not know whether the blood smears showed aplasia or regeneration; but it certainly is very uncommon, the hemolytic type of anemia being much more frequent.

What would be the autopsy findings which would prove whether my ideas are correct? I think that, if the patient died from a hemolytic anemia due to sulfanilamide, we should find a

hyperplastic bone marrow so far as the red-cell series is concerned and, in addition, evidence of arrested maturation of the white-cell series. This is usually found in cases of agranulocytosis due to drugs, and from the few cases that have been autopsied, sulfanilamide is no exception. In other words, the bone marrow will not show a complete depression of the white-cell series but only an arrested maturation, with mostly blast cells. In addition, the hemolytic nature of the anemia should be evidenced by the deposition of iron-containing pigment in the reticuloendothelial system in the liver and spleen. That would be my explanation as to the cause of her death — that it was largely due to toxicity from sulfanilamide rather than primarily to the urinary infection or to the diabetes.

DR. MAURICE-FREMONT SMITH: I am interested in the low liver function. Do you usually get that with secondary anemia from any cause?

DR. TRACY B. MALLORY: Not so low as that.

DR. SHORT: Low liver function has been reported in cases of severe hemolytic anemia due to sulfanilamide.

DR. WYMAN RICHARDSON: I predict that some day we shall see toxic hepatitis from sulfanilamide.

DR. SHORT: Toxic hepatitis has been described as due to sulfanilamide, but in this case I should think it was bringing in an extra factor that is not necessary.

CLINICAL DIAGNOSES

Toxic hepatitis.
Diabetes mellitus.
Bacillus coli pyelitis.
Agranulocytosis.

DR. SHORT'S DIAGNOSES

Pyelonephritis.
Hemolytic anemia.
Agranulocytosis.
Diabetes mellitus.

ANATOMICAL DIAGNOSES

Chronic pyelonephritis, bilateral.
Perinephric abscess, right.
Cystitis, acute hemorrhagic.
Obesity.
Agranulocytosis.
Erythropoietic hyperplasia.

PATHOLOGICAL DISCUSSION

DR. MALLORY: The autopsy on this woman showed that there was an extremely severe bilateral pyelonephritis with multiple abscesses scattered throughout both kidneys, and on the right side one of these had perforated the capsule and a perinephritic abscess had developed anterior to the kidney, lying between the adrenal gland and the second portion of the duodenum. It was a rather extensive pencil-like tract, which was not very wide at any point. There was nothing in the clinical history that suggested it at all. I do not believe that anyone could have localized it or drained it.

The other finding of major interest was the condition of the bone marrow. That showed a definite hyperplasia of the red-cell series, which had extended even into the long bones. The marrow in the central part of the femur was quite markedly erythrogenic. There were a moderate number of undifferentiated cells, but most of them appeared to belong to the red-cell series, so far as we could identify them. The white-cell elements appeared to be completely and specifically eliminated. Megakaryocytes were present in normal numbers, and a moderate number of plasma cells were found. Whether on that basis we can decide that this agranulocytosis was or was not due to sulfanilamide, as Dr. Short suggests, I am uncertain, but my inclination is to believe that it primarily was.

DR. JAMES H. THORNDIKE: Did she have a fatal lesion in the kidneys?

DR. MALLORY: Yes, I think there is not the slightest doubt that she would have died of renal sepsis.

DR. EUGENE S. SULLIVAN: Do you remember whether the abscesses in the kidneys showed polymorphonuclears?

DR. MALLORY: None whatever. Cultures from them showed *Bacillus coli* and nonhemolytic streptococci.

DR. RICHARDSON: How about the liver?

DR. MALLORY: It showed essentially nothing. There was a good deal of hemosiderin in the bone marrow and spleen.

DR. SHORT: What is the possibility that there were blasts completely undifferentiated, but belonging to the white-cell series, in the bone marrow?

DR. MALLORY: The total cellularity of the bone marrow was about half normal, and the half that you could identify appeared to be wholly of the red-cell series.

DR. SHORT: Has that been your observation in the cases of agranulocytosis — arrested maturation rather than aplasia of the white-cell series?

DR. MALLORY: Usually, but I am sure I have seen both types of reaction.

I do not believe the autopsy findings can be considered conclusive one way or the other. I certainly do not believe that I can exclude the possibility that the agranulocytosis was due to the

sulfanilamide. On the other hand the amount of renal sepsis was, I am sure, enough to have been lethal; strenuous efforts were therefore justified in the attempt to control it.

CASE 26082

Presentation of Case

A sixty-four-year-old widowed Canadian nurse entered the hospital complaining of asthma.

Approximately three weeks before entry the patient had a chest cold associated with a slight cough, more pronounced at night, with the production of white, frothy, stringy, tenacious sputum. One week later she suddenly had an attack of difficulty in getting her breath both on expiration and inspiration, although this was seemingly more marked with the latter. A physician was called, and he gave her adrenalin, which relieved her. After that she had occasional similar but less severe attacks, which were controlled by capsules left by her physician. She was also taking an expectorant cough medicine at that time. She had a severe attack one week before entry, and another on the evening before entry which was so bad that she "nearly died" and required adrenalin. She had had two attacks of asthma during her life, both very slight. The first attack, thirty years before admission, was associated with smoke from stove polish, and the other, twenty-five years before entry, was without any known cause. She had lived in the same house for two years and had had a dog for ten years. She had always noted that she felt much better when at a high altitude. For the previous seven years during the month of August she had had hay fever. This was always relieved by going to Nova Scotia. She had never had any skin lesions and was not subject to food idiosyncrasies.

There was no family history of hay fever or asthma. She had been born in Nova Scotia, and all her life had been spent either there or in Massachusetts, except for several years in California. There was no history of pneumonia or pleurisy.

Physical examination showed a well-developed and rather thin woman in no apparent distress. The chest showed slight hyperresonance and was clear except for occasional diffuse squeaks and groans. The heart was not enlarged; the sounds were not remarkable. No murmurs were heard. There was slight accentuation of the apical first sound. The blood pressure was 165 systolic, 80 diastolic. The peripheral arteries were firm.

The temperature was 98°F., the pulse 82, and the respirations 22.

Examination of the urine was negative. The blood showed a red-cell count of 6,180,000, with a hemoglobin of 80 per cent, and a white-cell count of 10,300 with 60 per cent polymorphonuclears, 28 per cent lymphocytes, 8 per cent monocytes and 4 per cent eosinophils. The sputum was thick and mucoid and contained a few cocci but no blood. The stools were negative.

X-ray films of the chest showed diffuse thickening of the lung markings, without areas of consolidation. The diaphragm was low in position and limited in excursion. A sinus plate showed diffuse thickening of the lining membrane of all sinuses, with obliteration of the air cavities of the right ethmoids.

She continued to raise mucopurulent sputum. Adrenalin helped her a great deal, although the chest still had scattered sibilant rales. Intradermal tests showed a good-sized reaction to ragweed and smaller ones to grasses. The tests somewhat aggravated her asthma, but this was slowly relieved by adrenalin. During the evening of the tenth day she had a severe asthmatic attack. Her pulse was weak and rapid; cyanosis was marked. There was no relief from adrenalin. She was put into an oxygen tent, with improvement. The extremities were cold and cyanotic. Intravenous 10 per cent glucose, containing 1 cc. of adrenalin, gave no striking relief. The blood pressure fell to 90 systolic, 70 diastolic, and the pulse was 120. She rapidly failed and died the following evening.

Differential Diagnosis

Dr. Milton H. Clifford: The story on first reading seems to be consistent with a perfectly clear-cut case of a woman dying in status asthmaticus, without any complicating factors. In fact, it sounds altogether too direct a story to be sure of such a diagnosis.

Here is a woman who, so far as we know, had been perfectly healthy until the last month of her life, except that at intermittent times she had had allergic manifestations — many years ago in the form of asthma, and in the last seven years in the form of hay fever — which one gathers had not been severe enough to bring her to a physician. We do not know whether her present hospital entry was during the time of the hay-fever season; if so, one would, perforce, be pushed even more to the diagnosis of asthma. Moreover, an attack of asthma is not uncommonly precipitated by an upper-respiratory infection. Thus the history is entirely in favor of asthma.

The physical examination also seems to confirm this, in that it was essentially negative except for the hyperresonance of emphysema and the typical squeaks and groans. It is to be noted, however, that when she was seen at home there seemed

to be even more difficulty in inspiration that in expiration, contrary to what one usually expects. The examination of the heart is reported as essentially negative; accentuation of the first sound means little, and it would be impossible to read a story of mitral stenosis into such minimal findings. There is no mention of distention of the neck veins, of engorgement of the liver or of the inability of the patient to lie flat. One assumes, however, the absence, particularly of the last observation, means that she was not having cardiac orthopnea. Further, the temperature was normal, and so far as we know, it stayed at least essentially normal throughout her stay, a fact which is against a complicating infection.

The x-ray films of the lungs give negative confirmation, particularly helping to rule out the possibility of a foreign body or of a tumor in the mediastinal region. The sinus film was quite consistent with an allergic state, presumably with thickened membranes and, along with the normal white-cell count and temperature, with no active infection. Probably a nasal examination would have shown a vasomotor rhinitis.

The most interesting of the laboratory findings is the polycythemia, which is perfectly consistent with the pseudopolycythemia seen in asthma, although whether associated with dehydration or with compensatory increase in oxygen-carrying units, particularly in view of a comparatively low hemoglobin, I do not know. The blood smear does not help us much, except that the eosinophilia of 4 per cent is consistent with, if not lower than, what is often found. Again, the paucity of organisms in the sputum goes with the thick, mucoid, plugging secretion found in the asthmatic patient.

In considering other types of illness, diffuse thickening of the lung margin is suggestive of a much longer process than the story which we have, and could go with a mild degree of non-specific pulmonary fibrosis or with bronchiolitis obliterans. But a fatal degree of these would be unlikely with so short a history, at least without more suggestive evidence of a cor pulmonale and a more prolonged and febrile terminal stage. Furthermore, no mention is made of clubbed fingers to go with a chronic pulmonary condition.

A foreign body in the main bronchus is not ruled out, except that the sputum was at no time either purulent or bloody, nor were there definite areas of atelectasis. What plugging there was apparently must have been with spasm and possibly related mucous plugs. Friedländer's bacillus will cause a very thick tenacious sputum, but again the patient had no febrile course, and except for the short terminal stage, was apparently not unduly sick.

There is one other possibility. We presume that this woman had some hypertension with a systolic pressure of 165 at entry. We also are led to the assumption that she had at least some generalized arteriosclerosis, as noted in the firmness of the radial arteries. Could it be possible that during the severe asthmatic attacks, on the tenth day, she had a coronary infarction? Certainly this can occur without pain, and with marked dyspnea. One would think, however, that such dyspnea would be out of proportion to the squeaks and groans heard in the chest. The blood pressure fell, but this could have been due to shock in any situation, and not at all specifically to a coronary infarction. Cyanosis could have gone with either. One might expect varying irregularities of the heart rate or a suggestion of cardiac enlargement with an infarction. These would not be necessary, however, and no remark on the pulse, except its rapidity, is noted. I do not believe that this possibility can be either ruled in or out. An electrocardiogram might possibly have helped a great deal. The amount of peripheral shock she was in could have been present with status asthmaticus as well as with coronary infarction.

There is no mention as to whether she was given any of the opium derivatives before or during this stage of shock. To many of the asthmatic patients, particularly those with symptoms as severe as those this woman had, morphine or pantopon seems to be an aggravator or institutor of even more severe asthma. Thus, even if it were known that she had a coronary occlusion, unless it had been previously ascertained she was not sensitive to opium derivatives, it would not have been wise to use them.

We have repeatedly heard that patients do not die in an asthmatic attack. Several years ago Dr. Mallory told me that he had seen some 13 cases in the Massachusetts General Hospital, up to that time, who had died of no other findable cause than the bronchial spasm of asthma and the lungs distended with trapped air.

My belief is that this patient died of bronchial asthma, that she had some arteriosclerosis, and by guesswork only, that she did not have any coronary infarction.

Clinical Diagnoses

Bronchial asthma.
Chronic bronchitis.
Emphysema.
Terminal pneumonia.

Dr. Clifford's Diagnoses

Status asthmaticus.
Emphysema of lungs.
Arteriosclerosis, general.

Anatomical Diagnoses

Bronchial asthma.
Pyelitis, bilateral, moderate.
Cholelithiasis.
Arteriosclerosis, slight, aortic.
Leiomyomas of the uterus.
Pleuritis, chronic fibrous, left.

Pathological Discussion

Dr. Tracy B. Mallory: As Dr. Clifford has already intimated we have had in this hospital a considerable experience with fatal bronchial asthma. A significant number of cases die in and apparently of an asthmatic paroxysm. Other modes of death indirectly attributable to asthma are those from cor pulmonale and from emphysema or a combination of the two. It has been our experience that patients with very chronic persistent asthma of twenty or thirty years' duration rarely die in a paroxysm. Paroxysmal deaths are much more frequent in people who have had comparatively little preceding asthma and especially in people who develop asthma for the first time in their fifties and sixties. Although this woman had had apparently two widely separated single attacks of asthma earlier in her life, it is probably fair to class her in the latter category.

At autopsy the findings were entirely typical of a paroxysmal death. Like all the other cases the bronchial tree from the first subdivision of the primary bronchi down to the respiratory bronchioles was plugged with thick tenacious mucinous casts. The alveoli were uniformly distended to the maximal inspiratory degree, but there was no anatomic fusion of alveoli or other evidence of structural emphysema. The heart, despite the systolic blood pressure reading of 165, was quite small, weighing only 225 gm. It seems doubtful, therefore, if she could have had a significant degree of hypertension, and it is possible that the blood pressure reading was taken shortly after she had received adrenalin. There was certainly no cor pulmonale, since the right ventricle measured only 2 mm. in thickness. The coronary arteries were entirely negative. The only coincidental findings of any significance were a slight acute bilateral pyelitis and a stone in the gall bladder.

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THE BENZOL HAZARD

The industrial hazards of benzol have long been recognized and in recent years increasingly stringent precautions have been taken to minimize or prevent its untoward effects. Yet, from recent studies, it is distressingly apparent that the potential dangers of this chemical are not appreciated to the fullest extent and that the clinical and pathologic manifestations of benzol poisoning are by no means as simple and clear cut as they were once thought to be.

A provocative series of articles* in the *Journal of Industrial Hygiene and Toxicology* has brought to light a number of previously unsuspected facts. It has hitherto been the general consensus that chronic benzol poisoning was characterized by the syndrome of aplastic anemia, that its earliest manifestation was a moderate or severe leukopenia and that a vapor concentration of 100 parts per million was compatible with complete safety for the workers. In view of the recent studies referred to, some if not all these dicta must be discarded.

It would appear that, in certain cases at least, vapor concentrations of less than 25 parts per million were followed by death, and the authors state that it "is doubtful whether any concentration of benzol greater than zero is safe over a long period of time." It is therefore obvious that if benzol is to be used in industry, close medical supervision of all workers is of the utmost importance, and it is to be hoped that in the future an adequate substitute will be developed for this hazardous, though efficient, solvent.

Contrary to what is usually taught, the syndrome of aplastic anemia with its attendant leukopenia is not characteristic of benzol poisoning. Hunter and his associates found in their cases polycythemia and anemia, leukopenia and leukocytosis, leukemoid blood pictures and apparently even true leukemia. Regarding the last, Mallory states: "The evidence that chronic exposure to benzene produces leukemia in human beings is still incomplete, but it is accumulating at a rate and to a volume which command serious consideration."

It is further stated that the clinical symptoms and signs of chronic poisoning may appear after a prolonged latent period, during which the worker may not have been exposed to the chemical, and it is suggested that under certain circumstances "industrial compensation must be extended to include cases of poisoning long after exposure has ceased." It is well to remember, however, that the *post hoc ergo propter hoc* argument has been and always will be uncertain and that one should not be too hasty in attributing a given hematologic disorder to an exposure to benzol some years before.

One can no longer rely on leukopenia as the earliest sign of benzol poisoning, and the bone marrow may apparently be aplastic, hyperplastic,

*Benzene (Benzol) Poisoning: Five papers. Reprinted from the *Journal of Industrial Hygiene and Toxicology* (21:321-435, 1939). 114 pp. Boston: Journal of Industrial Hygiene and Toxicology, 1939. Bound reprints of three papers in this series, "Chronic Exposure to Benzene (Benzol). I. The Industrial Aspects. II. The Clinical Effects. IV. The Pathological Results," are available for distribution to Massachusetts physicians on application to the Division of Occupational Hygiene, Department of Labor and Industries, 23 Joy Street, Boston.

leukemoid or even deceptively similar to "the neoplastic processes termed Hodgkin's sarcoma."

According to Hunter's findings, benzol poisoning must be suspected whenever, in an exposed person, an eosinophilia exists, whenever the percentage of polymorphonuclear neutrophils is decreased or whenever young white blood cells are present in the peripheral blood; and the earliest diagnosis must depend on an evaluation of the complete blood picture rather than any particular hematologic feature. The diagnosis must be made, or at least suspected, before anemia develops, if a favorable outcome is to be expected.

It is clear that the former criteria for the clinical and pathological diagnosis of benzol poisoning must be revised. It would appear that a large variety of hematologic syndromes may follow exposure to benzol, even in minimal concentrations. The clinical and industrial implications of these facts are far-reaching and of the greatest importance.

A GOVERNMENTAL SYPHILIS PROJECT

A LETTER in this issue of the *Journal* calls attention to a governmental activity in the field of medicine which has been going on in Boston since 1937. The syphilis problem is large enough to demand a careful investigation from every possible angle. The best results can be obtained by the cooperation of all possible organizations in a particular region. It is quite necessary that any such survey be undertaken by individuals with adequate experience in syphilis and in the interpretation of the records of such cases. In the case of the records themselves, there are undoubtedly periods in any hospital when the records are not accurate, perhaps by reason of insufficient personnel or by reason of changes or additions to personnel, particularly that brought about by new individuals coming into the hospital for training.

Any such survey should be under the careful direction of the hospital staff in addition to the personnel of the project, because the members of the former are usually much more familiar with the patients and problems of the clinic. Such cooperative studies of the end results of syphilis, carried on with definite assurance of proper supervision and of a satisfactory technic for developing the desired statistics, should furnish considerable information with regard to the status of syphilis in a particular community.

MEDICAL EPONYM

BASEDOW'S DISEASE

The description of exophthalmic goiter which is considered classic by the Germans is that of Karl A. von Basedow (1799–1854), a practicing physician in Merseburg. It appeared in Casper's *Wochenschrift für die gesammte Heilkunde* (197–204, 220–228, 1840). The article is entitled "Exophthalmos durch Hypertrophie des Zellgewebes in der Augenhöhle [Exophthalmos as a Result of Hypertrophy of the Cellular Tissue of the Orbit]." The translation of a portion of the article is as follows:

> I have frequently observed exophthalmos caused by . . . a diseased condition of the cellular tissue of the orbit—a peculiar hypertrophy which seemed to arise as the result of disease of the heart and the larger blood vessels of certain glandular and other tissues.
>
> Fourteen years ago I first made the acquaintance of Mrs. G., when she was a nineteen-year-old girl. At that time she was still suffering from scrofulous glands in the neck, but was otherwise well. She had had an acute rheumatism which had left, as sequelae, edema of the ankles, loss of weight, amenorrhea, palpitation and rapid small pulse, precordial distress and dyspnea. Even at this time there was also, however, a definite protrusion of the otherwise healthy and visually normal eyeball, so that the patient slept with the eyes open, had a frightened appearance, conducted herself in a careless and lively manner, and soon had the reputation of being a little mad.
>
> Coincident strumous swelling of the thyroid gland led me to suspect a similar intumescence of the cellular tissue behind the optic bulb and suggested the use of iodine and digitalis, whereupon an improvement in all her symptoms resulted . . . although she still showed an unhealthy pallor and her eyes were unnaturally wide open and prominent.

After detailing the typical symptoms of hyperthyroidism in four other cases, he concludes:

> Having given it as my opinion that the immediate cause of exophthalmos is a strumous hypertrophy of the cellular retrobulbar tissue, I wish to amplify this by saying that I regard this hypertrophy as an incidental phenomenon, secondary to an abnormal condition of the circulatory system—a blood dyscrasia which, by reason of some as yet unknown scrofulous taint, takes the form of glandular growths and tissue hypertrophy.

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

SECTION OF OBSTETRICS AND GYNECOLOGY*

RAYMOND S. TITUS, M.D., *Secretary*
330 Dartmouth Street
Boston

SEPSIS DEVELOPING FIVE DAYS AFTER FORCEPS DELIVERY

Mrs. L. P., a twenty-one-year-old primipara, was admitted to the hospital February 13, 1933. She was at term but not in labor, and entered because of a slight bloody show.

The family history was negative, as was the patient's previous history. Catamenia began at fourteen, were regular with a twenty-eight-day cycle and lasted four days. The last period had begun on May 4, 1932, and confinement was expected about February 11.

The pregnancy had been characterized by much nausea during the first trimester. The blood pressure and urine had been consistently negative, and there had been no headaches or edema.

Examination on admission showed a well-developed and nourished woman. The temperature was 98.0°F., the pulse 88, the respirations 22, and the blood pressure 120 systolic, 80 diastolic. The heart sounds were clear, and the action regular; there were no murmurs. The lungs showed uniform resonance and were clear. The abdomen presented a full-term pregnancy, the fetus lying in an OLA position, with the head well engaged. The pelvic measurements were within normal limits.

Rectal examination showed no dilatation of the cervix. There was a slight discharge of blood-tinged mucus. Urine examination showed the slightest possible trace of albumin and no sugar; the sediment was essentially negative. A blood Wassermann test was negative.

After a twelve-hour labor the patient was delivered by a mid-forceps application on February 14. A right lateral episiotomy was done and repaired with No. 2 chromic catgut. The child, a boy, weighing 8 pounds, 11 ounces, was in good condition. The placenta was expressed after fifteen minutes; the uterus contracted well, and there was no undue bleeding.

The patient's temperature remained below 99.0°F. until the evening of the fifth day. There was at the time a definite epidemic of streptococcal infection in the hospital, and what were believed to be rigorous precautions were being taken to prevent its spread. On the evening of the fifth day the patient's temperature rose to 101.0°F., but the pulse was not affected. The fundus was well contracted, the lochia was not foul and the episiotomy wound appeared clean. Ice was applied to the fundus, an ampule of pituitary extract was given hypodermically, and half a teaspoonful of fluid extract of ergot was ordered to be given by mouth every four hours. The temperature continued to rise, reaching 104.0°F. on the ninth day.

The white-cell count on the sixth day was 16,800. The blood sedimentation rate by Friedländer's method was ten minutes, and the hemoglobin was 65 per cent (Sahli). A blood culture taken on the ninth day showed no growth, and cultures taken on the eleventh, fifteenth and seventeenth days post partum were also negative.

The temperature remained at 104.0°F. for two days and then dropped to 101. On the thirteenth day it rose to 103.0°F. and continued to show a picket-type course, its highest point being 105.0 and its lowest 98.0, for seven days, after which time it dropped to normal.

On the eleventh day the sutures were removed from the episiotomy wound; a small amount of pus escaped, but the temperature was not affected. The lochia became somewhat foul on about the seventh day post partum.

Treatment was conservative. Food and fluids were forced, and ice was applied intermittently to the fundus. Several courses of ergot by mouth were given. On the seventeenth day a transfusion of 250 cc. of citrated blood was given from a compatible donor. It was intended to follow this up with a series of small transfusions at intervals of a few days, but on the twentieth day the temperature dropped to normal and remained there during the rest of the patient's hospital stay.

The patient was discharged the twenty-third postpartum day. Discharge examination showed the uterus fairly well involuted, the vaults clear and the episiotomy wound clean although still granulating.

Comment. This is a case of institutional sepsis. Such cases may develop any time during the puerperium, this case showing no febrile reaction until the fifth day. Conservative treatment was followed. It is doubtful if the single transfusion had any effect on the course of the infection, although repeated small transfusions furnish one of the best ways of raising the patient's resistance. In cases of sepsis developing after three days it is presumable that the infection did not gain entrance at the time of delivery. It is possible that this infection was secondary to a throat in-

*A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section.

fection in the patient or was due to contamination following imperfect nursing care. In cases of epidemic infection all persons having anything whatever to do with the parturient patient should have throat cultures taken at least once a week and should be meticulous in the use of masks; furthermore, the care of utensils, bedpans and so forth must be scrupulous. As has been pointed out in this column before, the only way to combat institutional infection is perfect isolation, and if this cannot be obtained, closure of the institution is imperative.

DEATH

SHEA — MICHAEL I. SHEA, M.D., of Chicopee, died February 11. He was in his sixty-fifth year.

Born in Chicopee, he attended the local schools and Holy Cross College. He received his degree from Georgetown University School of Medicine in 1904 and later studied at Vienna. At the time of his death Dr. Shea was city physician and a member of the board of trustees of the Monson State Hospital. He was also chairman of the board of health and on the staff at Mercy Hospital.

Dr. Shea was a former member of the Massachusetts Medical Society.

His widow, two sons, two daughters, a brother and four sisters survive him.

MISCELLANY

GIFT FOR TUFTS

A gift of $42,200 to the Tufts College Medical School from Dr. and Mrs. George G. Averill, of Waterville, Maine, was recently announced by President Leonard Carmichael. The fund, to be turned over to the school during the years of 1940 and 1941, will be devoted to the establishment of the Dr. and Mrs. George G. Averill Department of Anatomy in Memory of Professor Charles P. Thayer, President Carmichael said. Known as an industrialist, Dr. Averill was one of the first physicians graduated from Tufts nearly half a century ago.

The new medical-school building, of which the gift will provide the entire top floor, will be situated in downtown Boston at the New England Medical Center, a location convenient to the Boston City Hospital and the other clinical teaching centers of the school, it was announced. It will be erected as soon as the entire $750,000 needed has been obtained. Dr. Charles P. Thayer, in whose memory the gift was made, was one of the original seven founders of the school in 1893 and first head of the anatomy department.

In a statement accompanying his gift, Dr. Averill said: "The Tufts College Medical School has attained a singular position of responsibility to New England; since my graduation nearly a half-century ago these six states have come to depend more and more for their medical care and community health services on Tufts. Now the school trains more physicians for New England than any other medical school in the country. In the same period, anatomy has attained recognition as a mother science, embracing all fields of medicine; it is important that students who will be the physicians of tomorrow have the best opportunity to study a subject which has become one of the major biological sciences concerned with life processes. As a New Englander I can think of no better investment than that which will support training at the school which is the chief source of our doctors."

RÉSUMÉ OF COMMUNICABLE DISEASES IN MASSACHUSETTS FOR DECEMBER, 1939

DISEASES	DECEMBER 1939	DECEMBER 1938	FIVE-YEAR AVERAGE*
Anterior poliomyelitis	6	0	5
Chickenpox	1510	1096	1495
Diphtheria	20	23	36
Dog bite	577	561	515
Dysentery, bacillary	26	14	7
German measles	26	55	122
Gonorrhea	335	400	517
Lobar pneumonia	396	415	447
Measles	1082	902	878
Meningococcus meningitis	1	5	8
Mumps	337	470	582
Paratyphoid B fever	2	6	2
Scarlet fever	412	506	768
Syphilis	433	480	443
Tuberculosis, pulmonary	284	177	253
Tuberculosis, other forms	28	23	28
Typhoid fever	5	3	8
Undulant fever	2	5	4
Whooping cough	511	784	839

*Based on figures for preceding five years.

RARE DISEASES

Anterior poliomyelitis was reported from: Haverhill, 1; Lynn, 1; Revere, 1; Saugus, 1; Somerset, 1; Worcester, 1; total, 6.

Diphtheria was reported from: Andover, 1; Boston, 3; Chelsea, 1; Dedham, 1; Foxboro, 2; Lawrence, 4; Methuen, 2; North Andover, 1; Revere, 2; Taunton, 3; total, 20.

Dysentery, bacillary, was reported from: Amherst, 1; Boston, 1; Brookline, 1; Cambridge, 3; Everett, 1; Lee, 3; Lowell, 1; Lynn, 3; Malden, 6; Medford, 3; Wrentham, 3; total, 26.

Infectious encephalitis was reported from: Boston, 1; total, 1.

Malaria was reported from Boston, 1; Taunton, 3; total, 4.

Meningococcus meningitis was reported from: Pittsfield, 1; total, 1.

Paratyphoid B fever was reported from: Brockton, 1; Peabody, 1; total, 2.

Pellagra was reported from: Gardner, 1; Haverhill, 1; total, 2.

Septic sore throat was reported from: Boston, 9; Braintree, 1; Cambridge, 1; Merrimac, 2; Milton, 1; New Ashford, 6; Williamstown, 2; total, 22.

Tetanus was reported from: Quincy, 1; total, 1.

Trachoma was reported from: Agawam, 1; Boston, 2; Brookline, 1; total, 4.

Trichinosis was reported from: Boston, 1; total, 1.

Typhoid fever was reported from: Agawam, 1; Boston, 1; Erving, 1; Newbury, 1; Weymouth, 1; total, 5.

Undulant fever was reported from: Gardner, 1; Wilmington, 1; total, 2.

For the first time in several months the reported incidence of diphtheria fell below that for the previous year.

Lobar pneumonia was reported well within the five-year average.

Bacillary dysentery, primarily of the Sonne type, continues to be prevalent, although at a lower level than for the past several months.

Scarlet fever had its lowest reported December incidence since 1918.

Dog bite had its highest reported December incidence.

Measles continued to show an increased incidence, reaching a figure above the five-year average.

There was nothing unusual about the reported incidences of anterior poliomyelitis, chickenpox, meningococcus meningitis, mumps, typhoid fever, paratyphoid fever, undulant fever, tuberculosis (pulmonary) and tuberculosis (other forms).

Whooping cough and German measles were reported well within the five-year averages.

NOTES

The following appointments to the staff of the Harvard Medical School have been recently announced: Hans P. Mueller, M.D., University of Koenigsberg, '31, of Koenigsberg, Germany, as assistant in roentgenology; Ping-Yang Liu, M.D., Hunan-Yale Medical College, '35, of Siangtan, Hunan, China, as research fellow in bacteriology and immunology; Carey M. Peters, M.D., Harvard, '36, of Spring Valley, New York, as assistant in medicine; Elias Strauss, M.D., Columbia, '37, of Roosevelt, New York, as research fellow in medicine; Herbert Lund, M.D., University of Pennsylvania, '31, of Uniontown, Pennsylvania, as research fellow in legal medicine.

John G. Scannell, a fourth-year student at the Harvard Medical School and the son of Dr. David D. Scannell, has been awarded the Henry Asbury Christian Prize, one of the outstanding honors of the Harvard Medical School. The prize is awarded to "the student in the fourth-year class who has displayed diligence and notable scholarship and offers promise for the future." The award was established in 1937 in honor of Dr. Henry A. Christian, Hersey Professor of the Theory and Practice of Physic, Emeritus, a member of the Harvard Medical School staff since 1902.

CORRESPONDENCE

SYPHILIS PROJECT

To the Editor: Project No. 17568 (Op. No. 665-14-3-493) was established by the Works Projects Administration in 1937 for the study of the problem of syphilis in Metropolitan Boston. This work has been carried on successfully at the Boston City Hospital, with the co-operation of the hospital authorities and members of the staff.

Many problems relating to syphilis have been undertaken, some of which have been satisfactorily dealt with while others are at present demanding the earnest attention of clinicians assisted by skilled technical workers. An analysis of the cost of syphilis in a large general hospital was published in the November 24, 1938, issue of the *Journal*.

A tremendous amount of material relative to syphilis and its management and end results has been collected, and after proper classification and evaluation, final deductions will be published.

On the basis of the findings in thousands of case records at the Boston City Hospital, research work has been done on tabes dorsalis, cerebral thrombosis and syphilitic involvement of the spinal cord. Extensive studies have been made on syphilis in pregnancy, syphilis and alcoholism, and cardiovascular syphilis. Syphilitic lesions of the eye, as described and diagnosed in case records at the Boston City Hospital, have been thoroughly studied and classified as to type, etiology, serology, therapy and outcome. Thousands of records of syphilitic cases have been abstracted. These abstracts have been transcribed to small cards that will be filed for future use by members of the hospital staff.

Bibliographic records relative to important contributions by the medical profession to the subject of syphilology have been prepared and filed in a convenient and easily accessible manner for ready reference.

Due to the inadequacy of the desired number of cases at the Boston City Hospital, and also because of the paucity of information pertinent to our specific interests in the records, it has been thought wise to extend the scope of the study of congenital syphilis.

A previously attempted study of the lesions in the long bones of syphilitic infants in the first six months of life has stimulated a widespread interest in the subject of congenital syphilis, and as a result it has been proposed by the heads of various hospitals in Metropolitan Boston to conduct a survey of congenital syphilis covering a period of twenty years. It is obvious that the results of a survey of such magnitude would be more truly reliable and decidedly more representative than would the results of the findings from a single hospital in any particular community.

The aims of the project in regard to the above proposal may be briefly summarized, as follows:

1. To investigate the frequency and time of appearance of changes in the long bones of congenitally syphilitic children.

2. To determine the value of modern antisyphilitic treatment in congenital syphilis.

3. To carry out a follow-up system, wherever possible, on those with congenital syphilis for the purpose of establishing the relative influence of modern antisyphilitic treatment on these patients with reference to their ultimate fate — physically, socially and economically.

4. To establish in each of the institutions mentioned a permanent file of the abstracted case records on congenital syphilis for the purpose of facilitating further research in the problem by the hospital staffs.

5. To investigate the importance of syphilis as a factor in the causation of stillbirths, and to establish more definitely the frequency of osseous and visceral lesions in these patients.

It must be emphasized, however, that one of the principal aims of the project is to assist in the accumulation and ultimate distribution of facts about the disease to the public, as its part in the nationwide campaign to eradicate syphilis.

MARY D. GASTON,
Project Supervisor.

Boston City Hospital,
Boston.

ARTICLES ACCEPTED BY THE AMERICAN MEDICAL ASSOCIATION COUNCIL ON PHARMACY AND CHEMISTRY

To the Editor: In addition to the articles enumerated in our letter of January 5 the following have been accepted:

Abbott Laboratories

Mixed Grass Concentrated Pollen Extract — Abbott (blue grass, orchard grass, timothy red top and sweet vernal grass, in equal parts)

Barry Allergy Laboratory, Inc.

Grass Mixture (Spring) Pollen Extract — Barry
Ragweed Pollen Extract — Barry

Mallinckrodt Chemical Works

Theobromine and Sodium Acetate — Mallinckrodt

Parke Davis & Company

Antipneumococcic Serum (Felton) Type I, Refined and Concentrated, 20,000 unit ambot package

Antipneumococcic Serum (Felton) Type I, Refined and Concentrated, 50,000 unit ambot package

Antipneumococcic Serum (Felton) Types I and II, Refined and Concentrated, 20,000 unit ambot package

Antipneumococcic Serum (Felton) Types I and II, Refined and Concentrated, 50,000 unit ambot package

Antipneumococcic Serum (Felton) Type II, Refined and Concentrated, 20,000 unit ambot package

Antipneumococcic Serum (Felton) Type II, Refined and Concentrated, 50,000 unit ambot package

The Smith-Dorsey Company

Emulsion Liquid Petrolatum, Chocolate Flavored

Emulsion Liquid Petrolatum, with ½ gr. Phenolphthalein per fluid ounce, Chocolate Flavored

Emulsion Liquid Petrolatum, with 5 gr. Phenolphthalein per fluid ounce, Chocolate Flavored

Frederick Stearns & Company

Thiamin Chloride Tablets — Stearns, 1.0 mg.

The Upjohn Company

Ampules Mercuric Salicylate, 0.065 gm. (1 gr.), 1 cc.

Ampules Mercury Succinimide, 0.02 gm. (⅓ gr.), 1 cc.

Ampule Solution Quinine and Urea Hydrochloride, 0.5 gm. (7½ gr.) 1½ cc.

PAUL NICHOLAS LEECH, *Secretary.*

535 North Dearborn Street,
Chicago, Illinois.

REPORT OF MEETING

SUFFOLK DISTRICT MEDICAL SOCIETY

A regular meeting of the Suffolk District Medical Society was held at the Boston Medical Library on November 29, with Dr. Reginald Fitz presiding. Drs. William Leifer, Louis Chargin and Harold T. Hyman, of New York City, spoke on "The Theory and Practice of Massive Dose Chemotherapy by the Intravenous Drip Method in the Treatment of Syphilis." In introduction, Dr. Hyman discussed the history of intravenous therapy in general, with particular reference to experiments which showed that many untoward reactions were the result of "speed shock" which stimulated nitritoid crises and anaphylactoid reactions. Due credit was given Dr. Rudolph Matas, of New Orleans, who first used the intravenous route of therapy in 1888.

Dr. Hyman went on to tell of the conditions of their clinical experiments with the intravenous method of treating syphilis by massive chemotherapy. All cases were studied by a special committee, and no patients were seen by the original group after the termination of the primary phase of the treatment. A six-bed ward was provided at Mt. Sinai Hospital where the early cases were confined for one week. Follow-up visits were made to specified clinics, for which one dollar was paid for each visit as an inducement. Triplicate blood specimens were collected for examination by recognized independent serologists. Upon return to the clinic, there was a complete physical examination, but no treatment was given to any case.

Dr. Leifer then discussed the technical details of the intravenous chemotherapy which was employed. Without any specific preparatory treatment, the patients entered the hospital, where they were immediately put to bed. A 20-gauge needle was used, and the injection was always made into a vein of the mid-forearm, so that a minimal amount of immobilization was necessary. After an initial infusion of 20 or 30 cc. of 5 per cent glucose solution, 0.1 gm. of arsphenamine in about 125 cc. of the same solution was allowed to run into the vein in about one hour. At this rate for ten hours on four successive days, an average dose of about 4 gm. was administered. The patients were allowed out of bed each evening unless there was some individual contraindication. The recipients were given the routine hospital diet and high-carbohydrate fluids were forced. Pretreatment studies consisted of a complete blood count, a platelet count, a determination of the nonprotein-nitrogen level, the urobilin content and a van den Bergh test. Measurements of the arsenic excretion showed that about 20 per cent was recovered in the urine and somewhat over 30 per cent in the stools. Studies on bilirubin excretion on 10 successive patients showed that 3 developed liver dysfunction. No patients showed any toxic or nitritoid reactions or local infiltration. However, 44 per cent developed a mild phlebitis, and 24 per cent moderate nausea and vomiting, usually with the "primary fever." A few had headache and diarrhea.

Two types of fever developed. The primary phase occurred about five to seven hours after the first injection and was accompanied by the above-mentioned symptoms. The phenomenon, which was similar to a Herxheimer reaction, was noted in 57 per cent of the patients, but the temperature always returned to normal the same evening or by the next morning at the latest. Continuation of treatment resulted in no exacerbations. The secondary fever, which usually appeared about the fifth day, had an incidence of 63 per cent, was accompanied by toxic cutaneous eruptions in some instances, and lasted from two to six days.

The dermatological reactions were usually noted on the sixth to the eighth day and were shown to be in no way benefited by 200 mg. of cevitamic acid daily. This toxicoderma, with an incidence of 52 per cent, was often accompanied by fever, headache and arthralgia. If previous antisyphilitic treatment had been given, its appearance was earlier.

Two patients showed clinical as well as laboratory evidence of jaundice, while a larger number showed evidence of subclinical jaundice in the form of an elevated icteric index and bile in the urine. This, however, compared favorably with the incidence of these conditions in the ordinary arsenical treatment of syphilis where 1 patient in 75 and 1 in 4 have clinical and subclinical jaundice, respectively.

A marked decrease of platelets occurred twice; but one patient had previously had thrombocytopenic purpura and was relieved by splenectomy, while the other had reacted similarly to other methods of arsenical therapy.

Daily urinalyses occasionally demonstrated a transient slight albuminuria which soon cleared. There were no significant casts, and the nonprotein-nitrogen level remained normal.

Probably the most significant toxic manifestation was

the polyneuritis which occurred in 32 per cent of the first group of patients and in 38 per cent of the second, despite the administration to the latter of presumably adequate amounts of thiamin chloride. The onset of symptoms was two to three weeks following discharge, and the mild symptoms and minimal signs persisted for three to six months. There was never any motor involvement, and only 4 of 86 patients were incapacitated during this period. All showed complete spontaneous recovery.

There was only one fatality, and the presence of a positive Pandy test was cited as probable evidence that a hemorrhagic encephalitis was the cause of death. Dr. Leifer added that there is the same mortality rate (1 per cent) in the usual forms of treatment and that the unfortunate result was probably due to an inherent specific sensitivity to the drug.

Dr. Chargin compared the results of their treatment with those of other types of antisyphilitic therapy. Satisfactory results were obtained in 89 per cent of 78 observed cases, as compared with the 80 per cent of favorable results in a typical series of continuously and alternately treated patients. There were no positive cerebrospinal-fluid findings in any case. The principal advantages of the method were its short duration and the small dosage of arsenicals necessary. It was even suggested that smaller total amounts of the drug might eventually be employed.

Dr. Hyman, in conclusion, enumerated the following advantages of the continuous intravenous method of treating syphilis: the patient is made non-infectious within forty-eight hours; 100 per cent of those starting the course of treatment finish; and the total arsenical dosage is small. He said that they believed that, with the exception of the polyneuritis, all the so-called toxic manifestations were merely evidence of sensitivity to the drug itself.

In opening the discussion, Dr. Nels A. Nelson lauded the method as a possible boon to the public-health management of syphilis but deplored the unfortunate publicity given it as a sure four-day cure for the disease, which he felt would bring unbearable pressure on the local physician to use the still experimental therapeutic procedure. He also desired to know the cost of such a procedure.

Dr. Hyman assured him that publicity was the last thing they desired. The cost of approximately $100 per patient was not considered a true criterion of the eventual cost since that included all experimental work.

The only criticism offered by Dr. William Boardman was that a follow-up of two or three years was not adequate, even in cases entirely asymptomatic and free of signs. The speakers granted that this was merely a preliminary report of a long-term experiment.

Dr. Austin Cheever was of the opinion that, as yet, the various reactions were too high to warrant the use of this method of therapy in a disease where 28 per cent of patients are cured without treatment and an equal number remain asymptomatic despite positive serological tests. The obvious answer by Dr. Chargin was that it is impossible to know who are to be the lucky ones.

In answer to a question from Dr. Marshall Crawford, Dr. Hyman replied that no correlation had been attempted with the work of Eagles, who showed that a relatively low concentration of arsenicals inactivated the *Treponema pallidum* in vitro. It was believed that too many additional factors play a role in vivo to make these results applicable in practical chemotherapy.

NOTICES

FAULKNER HOSPITAL

The monthly clinicopathological conference of the Faulkner Hospital will be held on Thursday, March 7, at 5:00 p.m. There will be a discussion of cases by Drs. James A. Halsted and Arthur R. Kimpton.

Physicians and medical students are cordially invited to attend.

UNITED STATES MARINE HOSPITAL

The staff meeting of the United States Marine Hospital, Chelsea, will be held at "The Hut," on Friday afternoon, March 1, at 4:00. Mr. John C. G. Loring will talk, his subject being "Neurotic Alcoholism."

MASSACHUSETTS GENERAL HOSPITAL

A meeting of the Hospital Research Council will be held in the Ether Dome of the Massachusetts General Hospital, on Tuesday, February 27, at 5:00 p.m.

PROGRAM

The Passage of Thiocyanate and Glucose from the Blood Stream into the Joint Spaces. Dr. J. W. Zeller.

Analysis of the Acoustics of the Stethoscope. Dr. H. B. Sprague and Mr. Maurice Rappaport.

Comparative Studies of the Effects of 200-Kilovolt and 1000-Kilovolt Roentgen Rays: The biologic effects on bone marrow, growing epiphyses and skin. Dr. E. A. Gall.

JEWISH MEMORIAL HOSPITAL

A meeting of the staff of the Jewish Memorial Hospital will be held in the hospital auditorium, 45 Townsend Street, Roxbury, on Thursday evening, February 29, at 8:30.

Dr. Joseph H. Pratt will speak on the subject "Pancreatic Disease." There will be an open discussion followed by a collation.

The medical profession is cordially invited to attend.

HARVARD MEDICAL SOCIETY

The next meeting of the Harvard Medical Society will be held on Tuesday, February 27, in the amphitheater of the Peter Bent Brigham Hospital (Shattuck Street entrance), at 8:15 p.m.

PROGRAM

Presentation of cases.

The Life History of Bone Grafts: Experimental and clinical observations. Dr. Ralph K. Ghormley, Mayo Clinic, Rochester, Minnesota.

Medical students and physicians are cordially invited to attend.

BOSTON DISPENSARY

A luncheon meeting of the clinical staff of the Boston Dispensary will be held on Tuesday, February 27, in the auditorium of the Joseph H. Pratt Diagnostic Hospital at 12 o'clock noon. The subject of the meeting will be "The New England Medical Center: Its origin, present activities and future plans" by Mr. Arthur G. Rotch.

This meeting will inaugurate a series of talks on the past, present and future of the New England Medical Cen-

ter and its component parts. Talks in the following months will be given by Dr. Charles C. Cabot and Mr. Frank E. Wing on the Boston Dispensary, Dr. Leonard J. Carmichael on the Tufts College Medical School, Dr. Elmer W. Barron on the Boston Floating Hospital and Dr. Joseph H. Pratt on the Pratt Diagnostic Hospital.

Luncheon will be served to non-members at 35 cents. All interested persons are cordially invited to attend.

PETER BENT BRIGHAM HOSPITAL

A joint medical and surgical clinic at the Peter Bent Brigham Hospital will be held on Wednesday, February 28, from 2 to 4 p.m. Drs. Lyman Richards and Soma Weiss will speak on "Sore Throat."

Physicians and students are cordially invited to attend.

PETER BENT BRIGHAM HOSPITAL

A research conference of the medical staff of the Peter Bent Brigham Hospital will be held in the amphitheater of the hospital on Tuesday, March 5, at 5:00 p.m.

PROGRAM

Blood and Urine Iodine in Diabetes Insipidus. Drs. H. H. Blotner and H. J. Perkin.

Further Observations on Dynamics of Circulation in Patent Ductus Arteriosus. Dr. E. C. Eppinger.

All interested persons are cordially invited to attend.

NEW ENGLAND SOCIETY OF PHYSICAL MEDICINE

There will be a meeting of the New England Society of Physical Medicine at 8:00 on Wednesday evening, February 28, at the Hotel Kenmore, Boston. An informal dinner will be held in the Empire Room at 6:30.

PROGRAM

Symposium on the Treatment of Arthritis.

1. Orthopedics. Dr. L. T. Swaim.
2. Diet and Hygiene for the Arthritic. Dr. J. P. Bill.
3. The Use and Abuse of Physical Agents. Dr. H. A. Osgood.

All members of the medical profession are cordially invited to attend.

EDWARD K. DUNHAM LECTURES

The Faculty of Medicine of Harvard University has announced that the following lectures will be given by Dr. S. Walter Ranson, professor of neurology and director of the Institute of Neurology, Northwestern University Medical School, Chicago, under the Edward K. Dunham Lectureship for the Promotion of the Medical Sciences:

Monday, March 4. The Hypothalamus and the Sympathetic Nervous System.

Wednesday, March 6. Hypothalamicohypophysial Relationships.

Friday, March 8. The Hypothalamus and Behavior.

These lectures are scheduled for 5:00 p.m. at the Harvard Medical School, Amphitheater, Building C.

NEW ENGLAND PATHOLOGICAL SOCIETY

The meeting scheduled for February 15 was not held because of the storm and has been rescheduled for Thursday, February 29, at 8:00 p.m. at the Tufts College Medical School, 416 Huntington Avenue, Boston.

PROGRAM

Pathological Observations in Simmonds' Disease. Dr. R. C. Wadsworth.

Immediate Wheal and Erythema Type Reactions to Simple Chemical Substances. Dr. John Jacobs.

Pathological Findings in Leukoerythroblastic Anemia. Dr. S. B. Thorson.

Primary Tumor of the Heart. Dr. Harold Wood.

The pathological demonstrations will be available at 7:00 p.m. There will be a short business meeting followed by a collation.

Physicians and students are cordially invited to attend.

NORFOLK DISTRICT MEDICAL SOCIETY

The regular meeting of the Norfolk District Medical Society will be held in the Hotel Somerset, Boston, Tuesday evening, February 27, at 8:30. Tel. KEN 2700.

PROGRAM

Business.

The Uses and Abuses of Sulfanilamide and Related Compounds. Dr. Chester S. Keefer. Discussion will be opened by Dr. John F. Casey.

Collation.

AMERICAN PHYSICIANS' ART ASSOCIATION

The American Physicians' Art Association, composed of over eight hundred physicians in the United States, Canada and Hawaii who follow some form of fine or applied art as an avocation, will hold its next annual art show at the Belmont-Plaza, New York City, June 10–14, during the annual session of the American Medical Association. All physicians, in active practice or retired, who have an art hobby, including photography, are cordially invited to participate in the New York exhibit.

A physician may join this association by mailing a check for one dollar to the treasurer, Dr. R. W. Burlingame, San Francisco County Hospital, San Francisco, California, briefly stating what art medium the applicant follows. For detailed information kindly write to the executive secretary, Dr. F. H. Redewill, 526 Flood Building, San Francisco, California.

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING SUNDAY, FEBRUARY 25

SUNDAY, FEBRUARY 25

4 p.m. Sterility (lecture for women only). Dr. Donald Macomber. Free public lecture. Harvard Medical School, amphitheater of Building D.

4 p.m. Surgery of the Blood Vessels and Extremities. Dr. B. Everett O'Neil. Illustrated, public, health lecture. Faulkner Hospital auditorium.

MONDAY, FEBRUARY 26

*8:15 p.m. New England Heart Association. Children's Hospital, Boston.

TUESDAY, FEBRUARY 27

*9–10 a.m. Suppurative Disease of the Lungs. Dr. L. F. Davenport. Joseph H. Pratt Diagnostic Hospital.

*12 m. The New England Medical Center: Its origin, present activities and future plans. Mr. Arthur G. Rotch. Boston Dispensary.

5 p.m. Hospital Research Council, Massachusetts General Hospital, Ether Dome.

*8:15 p.m. The Life History of Bone Grafts: Experimental and clinical observations. Dr. Ralph K. Ghormley. Harvard Medical Society, Peter Bent Brigham Hospital (Shattuck Street entrance).

8:30 p.m. The Uses and Abuses of Sulfanilamide and Related Compounds. Dr. Chester S. Keefer. Norfolk District Medical Society. Hotel Somerset, Boston.

WEDNESDAY, FEBRUARY 28

*9–10 a.m. Hospital case presentation. Dr. S. J. Thannhauser. Joseph H. Pratt Diagnostic Hospital.

*2–4 p.m. Sore throat. Drs. Lyman Richards and Soma Weiss. Peter Bent Brigham Hospital.

*8 p.m. New England Society of Physical Medicine. Hotel Kenmore, Boston.

THURSDAY, FEBRUARY 29

*9–10 a.m. Derangements of the knee. Arthur A. Thibodeau. Joseph H. Pratt Diagnostic Hospital.

5 p.m. Renal Physiology. Dr. Donald D. Van Slyke. Harvard chapter of Nu Sigma Nu. Harvard Medical School, Building E.

*8 p.m. New England Pathological Society. Tufts College Medical School.

*8:30 p.m. Staff meeting. Jewish Memorial Hospital. 45 Townsend Street, Roxbury.

*Open to the medical profession.

FEBRUARY 22–24 — American Orthopsychiatric Association. Page 957, issue of December 14.

FEBRUARY 23 — Staff meeting. United States Marine Hospital. Page 284, issue of February 15.

FEBRUARY 25 — Public lecture. Salem Hospital. Page 1042, issue of December 28.

FEBRUARY 25 — Free public lecture. Quincy City Hospital. Page 77, issue of January 11.

MARCH 1 — Staff meeting. United States Marine Hospital. Page 331.

MARCH 2, JUNE 8 and 10 — American Board of Ophthalmology. Page 719, issue of November 2.

MARCH 4, 6 and 8 — Edward K. Dunham Lectures. Page 332.

MARCH 5 — Research Conference of the Medical Staff. Peter Bent Brigham Hospital. Page 332.

MARCH 7 — Clinicopathological conference. Faulkner Hospital. Page 331.

MARCH 7–9 — New England Hospital Association. Hotel Statler, Boston.

MARCH 14 — Pentucket Association of Physicians. 8:30 p.m., Hotel Bartlett, Haverhill.

APRIL 15–17 — American Association for the Study of Goiter. Page 203, issue of February 1.

APRIL 15–19 — New England Health Institute. Page 284, issue of February 15.

APRIL 24–26 — Scientific Session. Academy of Physical Medicine. Hotel John Marshall, Richmond, Virginia.

MAY 10–18 — American Scientific Congress. Page 1043, issue of December 28.

MAY 13 — United States Pharmacopoeial Convention. Page 202, issue of February 1.

JUNE 7–9 — American Board of Obstetrics and Gynecology. Page 1019, issue of June 15.

JUNE 10–14 — American Physicians' Art Association. Page 332.

DISTRICT MEDICAL SOCIETIES

ESSEX SOUTH

MARCH 6 — Experimental and Clinical Considerations of Sulfanilamide Treatment of Hemolytic Streptococcus Infections. Dr. Champ Lyons. Lynn Hospital, Lynn.

APRIL 3 — Addison Gilbert Hospital, Gloucester.

MAY 8 — Annual meeting. Salem Country Club, Peabody.

FRANKLIN

MARCH 12 — Franklin County Hospital, Greenfield.

MAY 14 — Franklin County Hospital, Greenfield.

HAMPSHIRE

MARCH 13.

MAY 8.

Meetings are held at 11:30 a.m. at the Cooley Dickinson Hospital, Northampton.

MIDDLESEX EAST

MARCH 20.

MAY 15.

Meetings are held at 12:15 p.m. at the Unicorn Country Club, Stoneham.

MIDDLESEX NORTH

APRIL 24.

JULY 31.

OCTOBER 30.

NORFOLK

FEBRUARY 27 — Page 332.

NORFOLK SOUTH

MARCH 7.

APRIL 4.

MAY 2.

All meetings, with the exception of one which is usually held at the Quincy City Hospital, are held at the Norfolk County Hospital in South Braintree, at 12 o'clock noon.

PLYMOUTH

MARCH 21 — Goddard Hospital, Brockton.

APRIL 18 — State Farm.

MAY 16 — Lakeville Sanatorium, Lakeville.

SUFFOLK

MARCH 27 — Scientific meeting. Symposium on Ulcerative Colitis and Diarrheas. Under the direction of Dr. Chester M. Jones.

APRIL 24 — Annual meeting in conjunction with the Boston Medical Library. Election of officers. Program and speakers to be announced later.

MAY 2 — Censors' meeting. Page 244, issue of February 8.

WORCESTER

MARCH 13 — Worcester Memorial Hospital.

APRIL 10 — Worcester Hahnemann Hospital.

MAY 8 — Worcester Country Club.

Each meeting begins with a dinner at 6:30 p.m. and is followed by a business and scientific meeting.

BOOK REVIEWS

The Evolution and Organization of the University Clinic. Simon Flexner. 41 pp. New York: Oxford University Press, 1939. $1.25.

Two lectures given at the Nuffield Institute in Oxford in January, 1938, by the Eastman Visiting Professor have been published in pamphlet form. They are distinctly worthy of preservation for much of the history of the development of the university clinic is contained in Dr. Flexner's brilliant review of this subject. As historical documents, these lectures are invaluable. Beginning with the first teaching laboratory of modern times, founded by Liebig in 1825, one is carried through the development of the university laboratory by Purkinje in 1842 and von Ziemssen in 1884 to the period of Virchow, Müller and Schönlein. Schönlein was followed by Frerichs and later by Traube and many others. American developments came much later. The first was that of Bowditch, a pupil of Ludwig, at the Harvard Medical School in 1871, and five years later, Johns Hopkins University established a laboratory in biology, including physiology, for Newell Martin, a pupil of Huxley and Foster. In 1889, the year the Johns Hopkins Hospital was opened, most diagnostic laboratories were attached to the wards, but in 1893, with the founding of the medical school, laboratories were established in relation with the preclinical sciences. The first actual hospital, built wholly for research in clinical medicine, was that established by the Rockefeller Institute in 1910, in which Welch took a leading part. The latest addition to the long list of laboratories now established is that of the Nuffield Institute, established by Lord Nuffield, long a friend of medicine. It seems not unlikely that the idea was implanted in Lord Nuffield's mind by Osler soon after he went to Oxford in 1905. The new laboratories with their full-time professorships should become an important center for medical research. No one could give them a happier start in medicine than Simon Flexner. These two lectures should be widely read by the medical profession in general.

Hospital Public Relations. Alden B. Mills. 361 pp. Chicago: Physicians' Record Co., 1939. $3.75.

This book reflects the changing attitude of the public toward hospitals and of the hospitals toward their communities. Time was when hospitals were regarded with dread; now they offer hope and inspire confidence. In the first chapters Mr. Mills sets forth some of the rea-

sons for this change of opinion, and the remainder of the book is devoted to showing why hospitals should explain themselves to the public and, since there is a right way and a wrong way, how it should be done. Inasmuch as hospital ethics closely follow medical ethics, it is necessary to remember that any public-relation program must respect the privacy of the patient and that the institution must avoid what might be termed advertising. Of course, one of the prime motives of public relations is to obtain support for the hospital, not only financial but also moral. In either case the program must be carefully prepared and thoroughly carried out. Careless and hasty planning and half-hearted or slipshod presentation spell failure.

The second part, which deals with methods of application of the theories of public relation set forth in the preceding chapters, contains a most complete and detailed list of the various ways of presenting the hospital's case to the public and also just how it should be done. Annual reports, pamphlets, letters, newspaper articles, motion pictures and radio programs are mentioned and explained. The chapter on fund raising should be read by all who contemplate such a campaign.

This book can be read with profit by all hospital administrators. They will find many valuable and stimulating ideas, which are intelligently set forth, and will probably adopt and carry out many of them. Trustees will find it crammed with ideas, new to many of them, which are informative and are sure to prove helpful in their relations to the hospital personnel and particularly valuable in guiding the relation of their hospital to the public.

It is a well-written book by a man, trained in civic and social affairs, who served as executive secretary to the Committee on the Costs of Medical Care and who at present is managing editor of *The Modern Hospital*.

Surgical Applied Anatomy. Frederick Treves. Tenth edition. 748 pp. Philadelphia: Lea & Febiger, 1939. $4.00.

This work, crammed full of practical information tersely expressed, has reached its tenth edition. This revision is by Lambert Rogers, professor of surgery at the University of Wales, who states in the preface: "To be invited to prepare a tenth edition of this long-established textbook, and thereby follow such distinguished revisors as Sir Arthur Keith and the late Professor C. C. Choyce, was an honour not lightly to be declined, albeit a task from which one might reasonably have shrunk." Rogers has attempted to re-establish the original design of the work and to eliminate modifications which have crept into previous revisions. The sections on the eye, ear, nose and throat have been modernized by his colleagues at the Cardiff Royal Infirmary, Messrs. Parry and Owen. He has also incorporated nine illustrations from *Everyday Surgery*, written by himself and d'Abreu.

Although Treves's work was originally intended for the use of surgical students, induing "the dull items of anatomy with meaning and interest by the aid of illustrations drawn from common medical and surgical experience," it is a valuable reference book for practitioners. The treatment of certain human ailments requires a knowledge of anatomy. Without this knowledge the treatment of these conditions cannot be intelligent, it can be nothing more than the blind following of generally accepted rules. The medical man who practices by rules misses the stimulation which springs from the thoughtful contemplation of fundamental knowledge. His efforts to care for patients cannot long be characterized by that vigor and enthusiasm so vital in promoting comforting confidence.

A splendid double-column index of thirty-five pages, nearly two hundred illustrations, excellent typography and flexible covers make this small volume a handy reference book. It is highly recommended to all practitioners and students.

Illustrations of Regional Anatomy. E. B. Jamieson. Second edition. Seven sections, 305 pp. Sections I to V inclusive; Edinburgh: E. & S. Livingstone, 1937. Sections VI and VII; Baltimore: Williams & Wilkins Co., 1939. Complete set, $15.00.

Jamieson is senior demonstrator and lecturer in anatomy at the University of Edinburgh. In 1934 he published five small atlases of anatomical diagrams and drawings illustrating the central nervous system, head and neck, abdomen, pelvis and thorax. They were so well received and calls for illustrations of the limbs were so persistent, that the author has not only published two volumes to cover the extremities but has revised the entire work. This second edition consists of over three hundred loose-leaf plates, many in several colors, assembled in seven sections, with flexible cardboard covers (6½ by 8¼ in.).

The plates are beautifully done and a joy to study. As the diagrams and views for the most part differ from those found in general works on human anatomy, they constitute a valuable supplement to any such volumes the student may own. Their small size and compactness render them conveniently useful in the lecture room and laboratory. Their reasonable cost is another attractive feature. Individual sections may be purchased and vary in price from $1.50 to $3.50.

The Rectum and Colon. E. Parker Hayden. 434 pp. Philadelphia: Lea & Febiger, 1939. $5.50.

This book is a comprehensive treatise of the minor and major diseases involving the colon, rectum and anus. Primarily surgical in nature the accepted non-surgical procedures are discussed and indications given for the use of the various methods described.

The book is very well organized, and the illustrations, whether photographs or drawings, are clear and helpful; it is well written, detailed but not cyclopedic. Controversial subjects are given ample discussion, and the reader is always given a definite opinion as to the procedure indicated, based on the experience of the writer and his associates at the Massachusetts General Hospital.

The reviewer has no hesitation in recommending this book. It is sufficiently detailed to be of value and sufficiently practical to be helpful to the student, proctologist and general surgeon.

Baptism of the Infant and the Fetus: An outline for the use of doctors and nurses. J. R. Bowen. Fourth edition. 12 pp. Dubuque: The M. J. Knippel Co., 1939. 25c.

This pamphlet is most valuable for doctors and nurses, especially in hospital practice where all denominations are treated. Since religious practices and beliefs are very sacred to the communicants of various religions and since the doctor is in many instances considered a clergyman, he should familiarize himself with these procedures for the emergency. It is well prepared and can be absorbed at one reading.